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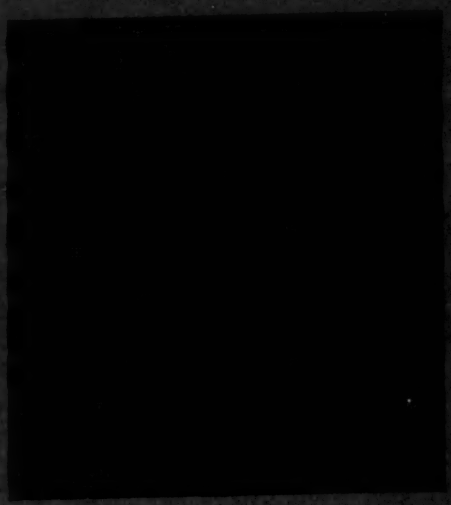

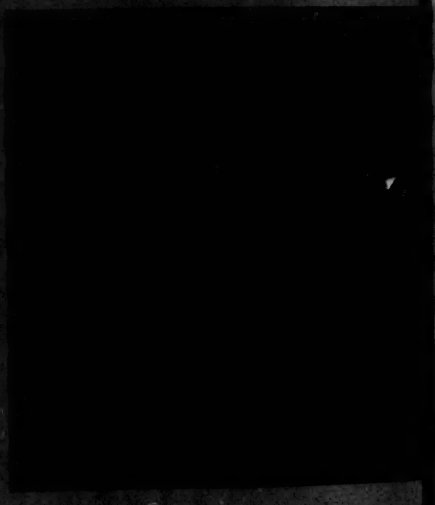

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THE BRITISH JOURNAL

OF

OPHTHALMOLOGY

SEPTEMBER, 1949

COMMUNICATIONS

SOME ASPECTS OF OCULAR MELANOTIC GROWTH*

BY

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IDA MANN (1926) stressed some years ago her conviction that the question of pigment origin must not be looked upon from the narrow sphere of ophthalmological pathology. Jean Nordmann (1947), indeed, has subscribed to this demand in an admirable way, so far as could be achieved in a short survey attempting to follow up the origin of the pigmented cells in the higher vertebrates. Relationship to light is one aspect, the influence of the hypothalamus another; such views are plentiful. Restriction to higher vertebrates appears to be dictated by sheer necessity.

Even the narrow ophthalmological outlook, however, offers a tremendous mass of unsolved puzzles involving embryology,

Dedicated to Professor J. Meller.

* Received for publication, August 19, 1948.

anatomy, physiology and, especially, pathology. The ophthalmologist's interest is certainly not limited to theoretical considerations as the growth of pigmented tumours engages our clinical interest so frequently. Basic difference of opinion is rife in the assessment of many pigmented growths, not only with regard to origin, but also to clinical behaviour and, last but not least, to treatment. Investigation of new material, especially if examined with varying technique, appears indicated in spite of the presence of a considerable literature covering this subject.

It is pigment production, the deposition of melanin, or one of the melanin substances, in these blastomata which dominates our attitude towards them. A non-pigmented wart growing at the lid margin would hardly worry us, while a pigmented new growth is the object of our justified concern.

Ribbert's conception (1911) of the mesodermic origin of the pigmented uveal growth remained unchallenged for years, and the malignant choroidal melanoma, the chromatophoroma, was considered as a melanosarcoma. This was hardly changed when T. W. Dawson (1925) and his Edinburgh school (E. K. Dawson, Innes and Harvey, 1939) tried hard to prove that these melanotic blastomata are ectodermal, and derive from the retinal pigment epithelium. Single cases of bulbus-filling melanotic masses of epithelial character have been described by Schuster (1918) and Pascheff (1929). Both assume an origin of the growth in the hexagonal layer. In recent years the name melanosarcoma—although still used clinically—is more and more abandoned in favour of the less committal " malignant uveal melanoma " as the shape of the tumour cells does not correspond frequently to the sarcoma type. Levkojeva (1940) found out of 202 malignant uveal blastomata only a small group which she considered as sarcoma type. We stress, however, here the fallacy of a decision reached from examination of routine sections, unless supplemented by flat sections or bulk examination of the cleared specimen.

A great change in the conception of pigmented growths came with Masson's papers (1926) which went back to Verocay's publication (1910). Verocay had shown that the neuro-fibromatous tumours in von Recklinghausen's disease were outgrowths from Schwann's sheath. Masson's revolutionizing work was concerned with the cutaneous naevus which he assumed to be a neural tumour, a Schwannoma. Schwann's cells are the melanin producing units, the melanoblasts. G. Dvorak-Theobald (1937) took up Masson's new idea and showed, investigating 6 malignant choroidal melanomata, that in 5 of them a tumour growth might have started in the long posterior ciliary nerves. Her paper influenced the English-speaking ophthalmological world in favour of Masson's theory.

She quoted Berger and Vaillantcourt (1934), who had already assumed that ocular melanomata are derivates from Schwann's cells. Nordmann (p. 116) is sure that uveal tissue generally is not simply mesodermal. Its mass of nerve fibres and nerve cells are closely interwoven with the pigment network. The malignant uveal blastoma is a special type of new growth in which choroidal melanophores and glial cells are a product of selective disintegration of Schwann's sheaths.

General pathologists and ophthalmologists were soon ready to accept the neuro-ectodermal theory of the origin of the naevus growth and consequently of the malignant uveal melanomata which were considered generally as neuro-ectodermal with no exception. Dawson's ectodermal theory was hardly mentioned in ophthalmological literature.

Eugene Wolff in his W. Mackenzie Memorial lecture (Glasgow, October 24, 1947) challenged the general validity of Masson's theory and added new material against it in a paper read at the meeting of the Ophthalmological Society, London, April 8, 1948. According to Wolff the naevus is regarded as a composite or mixed tumour consisting of naevus cells, epithelial cells and branched chromatophores. Each of these cell types may proliferate alone or with others and produce a malignant pigmented tumour. The final structure depends on the relative proportion of the three types of cells.

Wolff's lecture stimulated a revision of material which I had collected over some years, the pigmented benign naevi at the lid margin and limbus and the malignant pigmented types of these regions, the naevi from the iris and choroid and finally the frequent iridic and choroidal malignant melanomata. It will be understood that certain aspects only will be discussed, seen from the point of view of classification, pathogenesis, propagation, etc.

The first type of melanotic growth which deserves special attention is the so-called naevus cysticus. There was a dark patch on the left eye at the limbal conjunctiva of a 16-year-old boy which was observed growing during a few weeks. Prof. A. J. Ballantyne, to whom I am indebted for the specimen, excised the growth, which could be peeled off easily from the sclera. It started growing again after two years. The tumour consists of normal conjunctival tissue with many goblet cells. There are (Fig. 1, A and B) densely packed, mostly round, dark-stained naevus cells with hardly any plasm. There is no typical gland formation, but great numbers of cystic spaces, mostly empty, some containing a fibrinous substance. Mucicarmin staining shows many goblet cells filled with mucin, and mucin is proven to be within the cystic spaces. Epithelial bridges link the conjunctival epithelium with

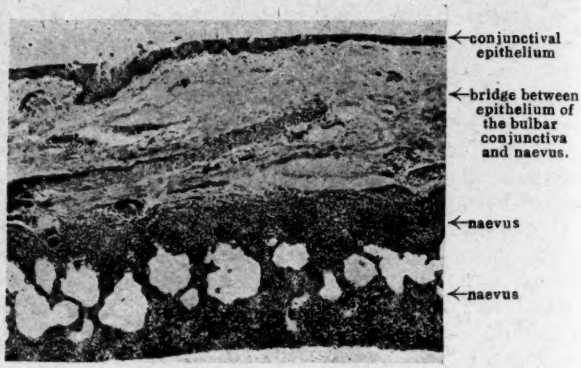

FIG. 1.

Naevus cysticus (M), at limbus area. H.E. 150×
Naevus cells with many mucous patches (goblet cells).

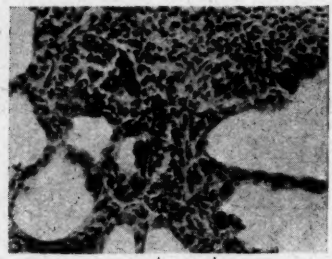

FIG. 1A.

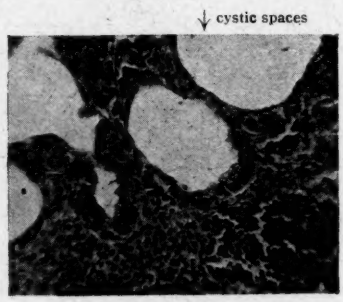

FIG. 1B.

Naevus pigmentosus cysticus. Mucicarmin staining. Note the (carmin red) swollen mucin containing naevus cells. 300×.

the naevus-cell tumour. There is a moderate pigmented content, best visible in unstained specimens. Cuenod and Nataf (1934) have shown several conjunctival cystic naevi in slit-lamp pictures.

The naevus nature of this growth is beyond doubt. So is the mucin production of its cells. The goblet cells within the tumour cannot be distinguished from those of the bulbar conjunctiva. The linkage between the conjunctival epithelium and the naevus growth is obvious. We do not doubt, therefore, that this type of cystic naevus appears to be derived from the epithelium as Unna (1893), Dawson (1925) and many others have assumed for the naevus generally.

There is another pigmented growth to be discussed which grew at the lid margin and appeared clinically as a pigmented rodent ulcer. It was excised in the whole thickness and the defect closed with a Buedinger-Mueller—whole thickness—auricle-flap (J. Foster). Histological investigation showed a naevus cell growth of unusual size which invaded (Fig. 2, A, B, C) the area of skin, Meibomian glands and palpebral conjunctiva. The epithelium of the skin as well as that of the conjunctiva has sent out down-growths of considerable depth of a controlled cell type. The majority of the naevus cells are typical, small, dark, without cytoplasm, and with a moderate pigment content. Some of the islets

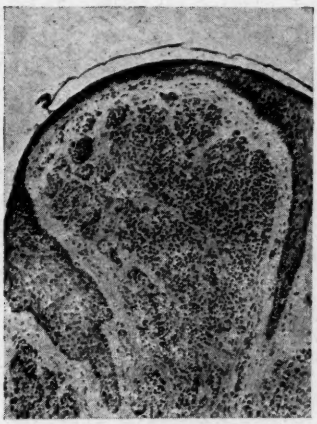

FIG. 2A.

Naevus pigmentosus of lower lid margin. H.E. 150×. Note thinning of epithelial cover over naevus growth and down growth of the skin epithelium at both sides of the naevus.

consist of larger cells with a clear plasm (Fig. 2, B) which have real epithelial character. Mucin reaction was negative everywhere except in the epithelial downgrowths of the conjunctiva.

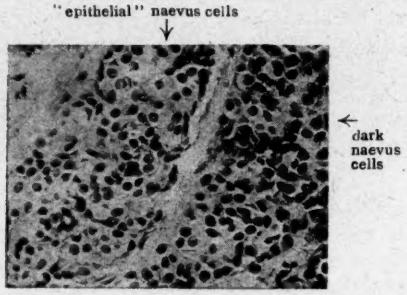

FIG. 2B.

Pigmented naevus at lower lid margin, H.E. 450×. Note the clear epithelial naevus islets to the left while the remaining naevus cells are dark with very little plasm.

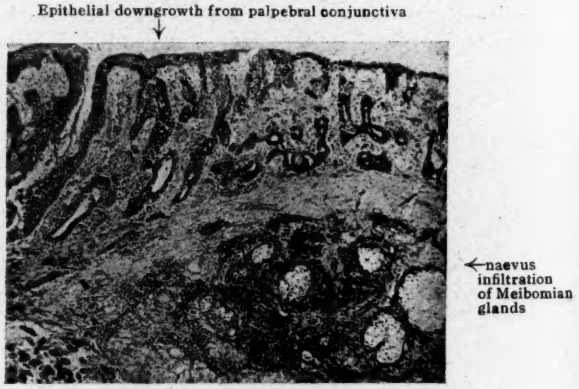

FIG. 2C.

Naevus pigmentosus of lower lid margin. H.E. 60×. The benign-looking naevus cells infiltrate the sebaceous glands. Note the downgrowth of the *conjunctival* epithelium.

The presence of both naevus cell types, the small, dark one with no cellular plasm, and the epithelial type side by side, is one point of interest. The other is the new growth of skin and conjunctiva which had created clinically the impression of a pigmented rodent ulcer. Our conception of this case is a primary growth of the

naevus cell explantate resting at the lid margin, probably since birth or earlier. It started growing at a certain age. We feel that this naevus cell growth is the stimulus for both types of *epithelial* outgrowth in conjunctiva and skin. Products of the naevus cell metabolism might work as growth promoting factors, as do the large groups of carcinogenous compounds. The "Melanins" are different chemically from all so far known carcinogenous substances.

Wolff's conception of the naevus as a mixed group of cells, typical naevus and epithelial cells, here seems to receive confirmation. Even branched chromatophores were present in small

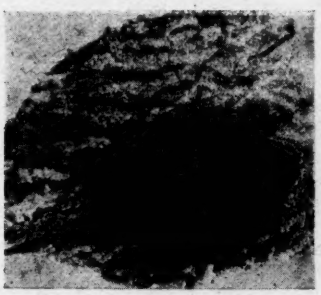

FIG. 3.

Choroidal naevus discovered by chance in flat choroid unstained seen from scleral side. 60× approx.

numbers, which might originate in the cells of Langerhans (Pascheff, 1946).

Choroidal naevi are certainly more frequent than we assume or than the scanty literature suggests. There is practically no possibility of a differential diagnosis between a beginning malignant melanoma and an innocent naevus, clinically. Such a diagnosis is frequently not even anatomically secured, as we shall show. Ophthalmoscopic control with repeated fundus photography seems to be the only way to discover the first sign of growth.

We were able to demonstrate two choroidal naevi anatomically, both found by chance in fixed, opened eyes, by routine slit-lamp examination. In neither case was a new growth, pigmented or unpigmented, present.

In the first case the dark choroidal patch was excised with a 4 mm. trephine, cleared in glycerine and photographed unstained (Fig. 3). Then the piece of choroid was embedded in paraffin,

cut and stained; depigmented slides showed the cell structure considerably better (Fig. 4).

The cell type is a spindle-cell form, denser in the outer choroidal layer, where pigmentation is heavier. The nuclei are of great inequality; although most of them are slim, they range from 2 to 15 μ in length, and from 2 to 5 μ in cross diameter. The pigment is in fine granules, round, resembling cocci of less than 1 μ diameter; where it is packed in branched melanophores it appears darker brown, but the size of the granules is still the same. The distinction from the rod-like retinal pigment in the same microscopic field is obvious. Some of the bigger " chromatophores " have no branches left. They are huge round cells packed with brown granules. Here we discover larger pigmented granules, which are caused, obviously, by fusion of the small equal granules. We have, therefore, to call the cells with the small

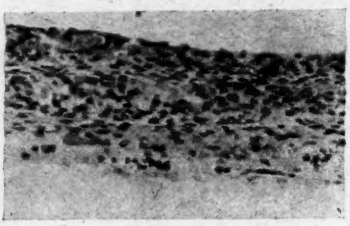

FIG. 4.

Choroidal naevus, depigmented. H.E. 300×.

brown granules of equal size melanoblasts, according to D. T. Smith (1925), while the bigger, heavier pigmented cells containing pigment granules of different size are chromatophores. The first produce the pigment granules, the latter store them.

The majority of these cells do not resemble a naevus-cell growth. They are mostly longer and spindle-shaped, that being the reason why older authors protested against the name choroidal naevus. Some cell groups of our two cases consist of small dark stained cells without cytoplasm, and are reminiscent of naevus cells of the skin. But we must not lay too much stress on the morphology of the cell type, generally. The great polymorphism of the melanoma cells is quite evident from the 14 different types of this blastoma distinguished in the classical work of Ernst Fuchs (1882). Even the retinoblastoma with its foetal, small, dark, round nuclei shows spindle-shaped cells in cases where the tumour has perforated the bulbar coats and grows in the soft orbital tissue.

This, indeed, was so striking that early authors spoke of a transformation of glioma to sarcoma. The tissue pressure undoubtedly exerts great influence upon the shape of the growing cells.

The choriocapillaris is nearly everywhere well preserved and Bruch's membrane intact. In our second case the structure of the growth is denser, the spindle cells are close together, the nuclei mostly dark stained, the pigment forms clumps, its granules are of different size, " melanoblasts " are absent. Branched chromatophores in the sclera are numerous, especially surrounding the pigmented ciliary nerve which joins the choroid in the naevus

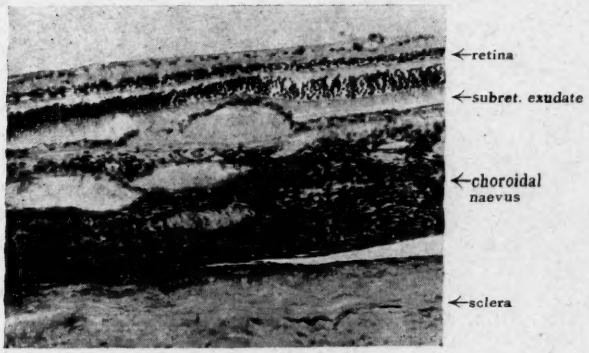

FIG. 5.

Choroidal naevus 2. H.E. 300×. Note: subretinal exudate over naevus.

area. While the greater part of the naevus leaves the choriocapillaris intact, there is a region where the naevus growth reaches Bruch's membrane and interferes with the choriocapillaris. Here a granular substance with eosin red shadows and empty vacuoles lifts the hexagonal cells (Fig. 5). It looks like an exudate between the intact Bruch's membrane and pigment epithelium. There is little doubt that this exudate is caused by the choroidal change, which here reaches its greatest intensity.

We have observed retinal disintegration frequently over choroidal malignant melanomata, even over small tumours (Fig. 6). It is interesting to note that this regressive process is present directly over the new growth and not over subretinal fluid often found adjacent to the tumour. This cystic degeneration of retinal tissue situated over a choroidal melanoma might be used diagnostically for tumour identification, as we have seen lately. We conclude that retinal nutrition might suffer when the vascular tissue

FIG. 6.

Malignant choroidal melanoma. H.E. 60× approx. Note cystic retinal degeneration over the tumour area exclusively. Not present over the serous detachment without tumour infiltration.

of the choroidal sponge is partly replaced by tumour growth. It seems interesting that a disturbance of such small size could be observed in a non-malignant growth of naevus character.

Anatomical investigation of these two choroidal naevi does not permit conclusive opinion as to the origin of these pigmented cells. At any rate, melanophores are present besides melanoblasts and the cells resemble a neurofibroma. We assume cell rests possibly of Schwannoma character, but we would not exclude displaced cells of the outer layer of the secondary eye vesicle.

We discuss a case of flat small malignant melanoma of mixed cell type with moderate histological malignancy and fatty necrosis. The small tumour was linked with the posterior ciliary nerve. The same cell type was present in the tumour tissue infiltrating the ciliary nerve. The branched chromatophores in the nerve tissue were especially well developed. Branched chromatophores were present in the sclera as well. Here we might assume the melanotic growth to have arisen from Schwann's sheath of the ciliary nerve. But it might be the other way; the malignant melanoma might have grown out from the choroidal tumour through the scleral emissarium following the line of least resistance. We are inclined to this conception, especially in a case of a more developed malignant melanoma in which huge contracted melanophores are amassed in the choroidal tumour and in the pigmented infiltrate of the ciliary nerve. The old conception of growth through the emissarium appeals especially in a case of big malignant melanoma which grew through the whole scleral thickness and ended in a black knob of about ¾ mm. diameter.

Loewenstein (1945) has described an interesting pigmented growth of the disc. This eye showed with other features a heavily

pigmented ciliary nerve entering the choroid where this tissue is thickened to twice its normal thickness. Nearly the whole choroidal tissue is formed by branched chromatophores. Between the dark pigmented chromatophores slim parallel arranged nuclei are visible of the same shape and size as the nuclei of Schwann's sheath in the adjacent posterior ciliary nerve. Loewenstein has explained the pigmented disc tumour as misplaced cells of the outer layer of the secondary eye vesicle, primitive cells, cell rests in the sense of Cohnheim, a phakoma with the inherent power of pigment production. Something similar might have happened in the same eye in the choroid where cell rests have produced a tissue belonging to the choroidal naevus group.

Summarizing our conception about choroidal naevi we assume the existence of cell rests possibly developmentally displaced. Schwann's cells might be the origin. The possibility that the outer layer of the secondary eye vesicle might be the source must be fully acknowledged. Both sources have the power of forming pigment. There is no reason to put the origin of malignant melanomata on another footing from the benign ones. Both types start in the outer layers of the choroid.

Wolff has found typical chromatophores in pigmented naevi of the conjunctiva. He identifies them with the mesodermal chromatophores (melanoblasts). We have seen similar structures in a malignant degenerated pigmented naevus at the limbus in flat sections and razor slides. We know fibroblasts of the conjunctiva have a great phagocytic power. The same is true of the cells of preretinal tissue. Seen in flat specimens these fibroblasts are branching and the tentacles are full of fat granules and pigmented corpuscles. They resemble, indeed, the choroidal chromatophores, especially those of the superficial layers. If we spread a choroid from a case of old chronic uveitis and stain it for fat with scarlet red the dendritic chromatophores are full of shining red fatty globules of different size and light brown pigment granules. We assume that these chromatophores have taken up pigment granules produced by the melanoblasts. The phagocytic power of these chromatophores is not exhausted by the absorption of pigment debris as they are able to absorb fatty droplets in addition. These cells belong, in our opinion, to the reticuloendothelial system, which forms another group of melanotic growth.

Loewenstein (1930) has seen a man of 41 years of fair complexion with no other clinical signs of a melanotic tumour. Small blackish nodules were discovered in the conjunctiva of all four of his lids. These nodules varied in size from 0·2 to 2·0 mm., they were mostly round or nearly so, one had a morular form. The conjunctival vessels surrounding the nodule were definitely

dilated. The colour of the pigmented nodules was not homogeneous, some were dark coffee brown, others light brown and some had a slight greenish hue.

The patient had used a collyrium once or twice daily for about ten years. It contained, besides zinc sulphate, adrenalin. No biopsy was possible. Animal experiment (rabbits) were performed. A collyrium with adrenalin was applied twice daily for a year without result. Subconjunctival injection for 18 months twice weekly approx., however, produced besides an increase in physiological epithelial pigment at the limbus, a group of blackish

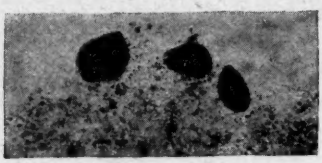

FIG. 7A.

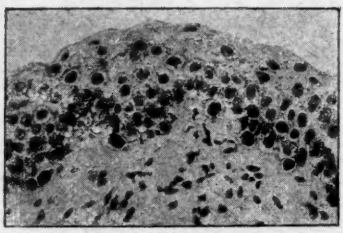

FIG. 7B.

nodules, similar, indeed, to those seen in the patient. Histologically (Fig. 7, A and B), there were melanin granules within the conjunctival epithelium, especially within the basal cells. Besides this epithelial pigment, there were many huge round or polyhedric reticulum cells filled with melanin granules.

The relationship of adrenalin and melanin is well established (Neuberg 1908). We know that homogentisinic acid is a product similar to adrenalin, and is the basic substance in alkaptonuria and ochronosis (deposits of melanin in many tissues). Naevus-like conjunctival pigmentation was shown by Cuenod and Nataf (1934) in a case of alkaptonuric ochronosis.

Similar melanotic changes in the conjunctiva have been described by Velhagen (1931) among workers in hydroquinone, a

substance belonging to the adrenalin group as well. Banks Anderson (1947) has published kodachromes of these melanotic changes in the conjunctiva, cornea and sclera in this industrial disease. Anderson's histological findings in biopsies are very similar to our own in the rabbit. He did not succeed in producing the changes in the animal experiment (continuation of the experiment was not long enough). Some lesions in the workers investigated by Anderson resembled the precancerous Bowen's disease, an observation which deserves careful consideration.

Describing precancerous melanosis Reese (1943) mentions varying numbers of cells in the submucosa, containing phagocytosed pigment. This might, according to Reese, originate in the basal epithelial layers. The exact mode of malignant transformation is not known. It seems to be the activity of basal epithelial layers from where the malignant proliferation spreads.

Observation of the adrenalin melanomata of the patient and of the rabbit has proved that adrenalin and its pigmented derivates are reabsorbed by the cells of the reticulo-endothelial system and stored. The same procedure seems to occur with hydroquinone workers. These little tumours are pigmented reticulo-endotheliomata. Future investigation may show whether they are the first stage of a malignant development or not.

The nature of the pigmented granules within the melanophores (or melanoblasts) is, unfortunately, completely obscure. Have they an independent life, reproducing by division, or are they a secreted end-product? It is of the same great interest whether, in the case of malignant melanoma, the pigment granules represent the tumour elements or only the innocent result of cellular disintegration. As far as is known this important problem is still unsolved. Pigment infiltration in the trabecular area and in the wall of the collector veins was demonstrated at Oxford in 1948.

We have investigated in a case of malignant melanoma of the iris and ciliary body the paths of elimination, from the anterior chamber. In one part of the specimen routine sections were performed. They showed (Fig. 8) the pigment growth in iris and ciliary body. The trabeculum is filled with a blackish mass. Schlemm's canal and collector veins are embedded in blackish granules. With oil immersion we can study the granules in the scleral part of a collector vessel. There are no cells visible, but granules of different size distributed in the wall of these "aqueous" veins (Ascher) in varying density. We get the impression that the pigmented detritus from the uveal melanoma suspended in the aqueous floated with the aqueous movement into the collector vessels. Many of these pigmented granules are taken up by reticulum cells.

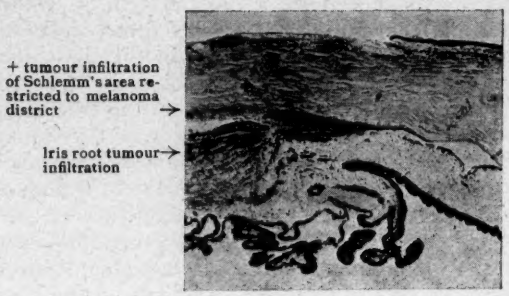

FIG. 8.

W., female. Malignant melanoma of iris root and ciliary body. H.E. 60×. The dark infiltration of the circulus venosus is restricted to the area of the uveal melanoma.

Mayou (1930) has shown a similar appearance in his first case, in which the area of Schlemm's canal was infiltrated with pigment. He attributes importance to this involvement since in his opinion it might be the only means of distinguishing an innocent from a malignant growth. Gonioscopic investigation of these cases appears indicated.

This type of distribution of the melanoma débris was even more evident with another kind of preparation. In the remaining tissue of the excised eye the uvea was removed by a cyclodialysis from the sclera and the anterior part, cornea and sclera, was cleared with wintergreen oil and studied unstained. Here the blackish infiltration of the drainage area is evident (Fig. 9). With

FIG. 9.

W.f. malignant melanoma of iris root and ciliary body. Hem. Cleared sclera and cornea. 60×. Seen from ant. chamber. Tumour infiltrated areas of trabecular network restricted to uveal tumour area. Pigment.

high power we recognise that the pigmentary granules are present along the aqueous veins (Ascher), but no cellular structures are visible. Although no metastatic cells are found the impression of a propagation of the melanoma along the drainage system is strong. This kind of pigment infiltration is different from the common one we find in cases of iridocyclitis, glaucoma or even in healthy eyes of elderly people. Here, the specimen is prepared in a similar way, the pigment in the endothelial cells of the trabeculum fibres is dirty-brown, of irregular shape, the product of wear and tear of the uveal tissue. We think that the pigmentary elements found in the anterior drainage system of the case of malignant melanoma in the anterior uvea might contain the living tumour granules. No definite decision is possible if based on anatomical findings exclusively.

The propagation of a choroidal malignant melanoma is even more complicated if we consider the reaction of the hexagonal cells. The pigmented cells of the retinal layer start growing into retinal tissue under varied conditions, so that pigment cells found in the retina in cases of malignant choroidal melanoma cannot be reasonably regarded as tumour cells.

We peeled off parts of the retina from several malignant choroidal melanomata, stained the pieces in bulk, cleared the tissue and studied the situation in the flat specimen. Retina can be separated from the tumour with difficulty only, but we succeeded at some places. The retinal tissue is infiltrated with huge dark cells where the tumour has broken into it. There is an outstanding polymorphism of these black chromatophores. Some are like typical clump cells of the iris, roundish, like amoebae which have drawn in their pseudopodia, others show

FIG. 10.

Case of malign melanoma of ciliary body and choroid. Retina peeled off and cleared (Hem.—150×). The pigmented cells are spreading within the retina especially along the retinal vessels.

branching processes. The granules are brownish to deep black. The chromatophores look different from those seen in bulk specimens of retinitis pigmentosa or chorioretinitis syphilitica. The propagation occurs along retinal vessels predominantly although free " clump cells " are frequent. Even massive migration along vessels (Fig. 10) can be demonstrated. Treacher Collins (1926) mentions in his report on " Melanomata of the Eye " this Ginsberg type of clump cells which rise from chromatophores undergoing malignant degeneration. This change of large branching uveal chromatophores into spherical or polygonal deeply pigmented cells without processes occurs according to Treacher Collins during a phase of deranged metabolism.

Bulk specimens of choroid are possible only at the outskirts of the melanoma, as no view can be achieved over a certain thickness of the specimen, even after long protracted depigmentation. Although the spindle-cell type predominates there a considerable polymorphism is to be observed. It seems that the different stages of contraction of the branched chromatophores are responsible for this polymorphism, for the explanation of which Treacher Collins' theory appears adequate. The amoeboid character of the chromatophores seems to be the main cause of the varying shape of chromatophores found with the melanomata, even in different parts of the same growth. Another reason is the reaction of the phagocytic reticulum cells engulfing pigment and other débris. These cells are protean, varying in shape, size and pigment content.

Finally, reference must be made to the special position of the hexagonal cells detached from this single layer. Pigmented epithelial cells are produced in great masses in many disorders of the uvea. They do not remain, practically, in a cell unit, as to create a kind of tumour, but are freed, swell, undergo fatty degeneration frequently and may extrude their whole content. This kind of production occurs at high velocity, as we do not usually discover any defect in the hexagonal layer despite the massive loss. Retinitis exudativa externa (Coats) is a typical example of this kind of hyperproduction and fatty changes, in which the mass of " ghost " or " bladder " cells might be taken for a blastomatous growth of this primitive layer, a blastoma as, *e.g.*, leukaemia is considered a tumour of the blood.

The true tumours of the hexagonal layers in the common sense might be expected in the shape of an epiblastic growth, a melanocarcinoma. We have seen, however, a growth of hexagonal cells in a case of dystrophia adiposa of the eyeball (Fig. 11), of undoubted fibromatous character. Here the fibroblasts grew out

from the hexagonal cells which produced therefore cells of mesodermal type. Here we want to stress the unique position of this primitive layer which remains, as far as can be observed microscopically, unchanged from early foetal life.

A similar behaviour of the epithelium of the lens capsule is recognized (Samuels, 1946 and otherwise) (Loewenstein, 1934), which produces under certain circumstances a fibroblastic tissue.

FIG. 11.

Dystrophia adiposa. H.E. 150×. The pigmented epithelium grows out into the fibroma-like tumour.

We conclude that hexagonal cells add a great variety of pigmented cells of very different shape to the pathological melanomatous growth in which even spindle-shaped units may be present. The presence of this type of cell, therefore, is no proof against the origin of a melanotic growth in the hexagonal layer.

SUMMARY AND CONCLUSIONS

(1) Naevi are generally inherited as are markings of domesticated animals (Meirowsky, 1942). They are developmentally arrested and often displaced tissues which might or might not, under unknown conditions, start multiplying from the point of development at which they have arrived. There is no basic difference between a naevus and a phakoma (Van der Hoeve).

(2) In tissues where these naevus cells produce pigment (melanoblasts), pigment granules are also stored in branched reticulum cells (melanophores).

(3) Pigmented naevi may be derived, as far as we know, from early stages of Schwann's sheath, from the primitive epithelium of the skin or from the outer layer of the secondary eye vesicle.

(4) No doubt exists about the epiblastic origin of the naevus mucosus cysticus of the conjunctiva.

(5) Pigmented naevus cell growth, at the margin of the lower lid, may contain, besides typical naevus cells, islets of epithelial structure and branched chromatophores.

(6) Naevus cell metabolism may set free growth-promoting factors responsible for controlled or uncontrolled new growth. These growth-promoting factors might be related to the melanins, being different from known carcinogenic substances.

(7) Distinction between innocent choroidal naevus and malignant choroidal melanoma is difficult ophthalmoscopically and histologically.

(8) The simultaneous presence of an identical pigmented melanoma in choroid and ciliary nerve is no proof of the origin of the blastoma from Schwann's sheath.

(9) There is a greater polymorphism of melanoma cells in flat sections and bulk specimens of melanoma invaded retina than in routine sections.

(10) Mesodermal structure of a pigmented malignant choroidal blastoma does not exclude origin in the hexagonal layers because out-growth from the pigmented epithelium may show typical mesodermal character. The unique developmental position of the pigmented epithelium, the outer layer of the secondary eye vesicle may account for this.

(11) The adrenalin melanoma is described clinically and histologically, and is explained, as is the conjunctival melanosis of the hydroquinon workers, by melanotic reticulosis. Although no malignant evolution is known, the corneal changes in hydroquinon damage are reminiscent of precancerous Bowen's disease. Adrenaline, hydroquinone and melanin are chemically related. Asthmatic persons receiving adrenaline for a long period ought to be observed carefully.

(12) Melanotic débris marked the path of elimination in cases of malignant melanoma of the iris. It is likely that the pigment granules in the trabeculum and vessels carry the tumour elements and show the course of the metastases. That might be a warning against "conservative" operation for localized malignant iris melanomata. Gonioscopic investigation of these cases before local excision of the melanoma is indicated.

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BLINDNESS ASSOCIATED WITH HAEMORRHAGE*

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DURING the syncopal phase which may accompany or immediately follow massive haemorrhage, it is not uncommon for the patient to complain of visual disturbances and even blindness. This condition is invariably brief and seldom exceeds one hour in duration. More often it only lasts a few minutes. Jones (1947) describes a typical case of this kind. (Also see Appendix.) Blindness of a longer duration and in most cases associated with permanent damage to the visual apparatus is a rare though well-recognised complication of massive and repeated haemorrhage.

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Although this latter variety of blindness may occur simultaneously with the haemorrhage, it occurs just as frequently after an interval of several days and even weeks. It would seem to be important to separate these two varieties of blindness in view of their different prognosis, and also in view of the fact that the former recovers with no therapy, whereas the latter variety has a uniformly bad prognosis in spite of treatment. These cases are not, however, clearly separated in the literature. It would seem that the former variety is associated with a rapid reduction in the blood-volume and a fall in blood-pressure. The latter or second variety would seem to occur when the blood-volume has returned to normal with the resulting fall in haemoglobin and plasma-proteins. However, there are other apparently essential requirements for the latter variety to occur, and they will be discussed more fully later in this paper. In the literature most of the described cases are of this second or delayed amaurosis, but for the purposes of the table in this paper they will all be grouped together, and where possible the date of onset after the last haemorrhage is given. Treatment has often been coloured by the physicians' ideas as to causation, and also limited by the means available to the earlier medical authorities who investigated the condition in any detail. Groenouw (1904) estimated that 25 per cent. of cases of amblyopia occurred during or immediately after haemorrhage, 20 per cent. occurred within 12 hours, and in more than 50 per cent. it appeared within three weeks of haemorrhage. Pergen (1896) said 21 per cent. of cases occurred simultaneously with the haemorrhage, 9 per cent. within twenty-four hours of bleeding, 51 per cent. within 7 days, 14 per cent. in the second week, and 5 per cent. in the third week. Terson (1922) from his collected cases gave 8·3 per cent. during haemorrhage, 11·6 per cent. immediately after haemorrhage, 14·2 per cent. within 12 hours, 19·2 per cent. within two days, 39·2 per cent. between three and sixteen days, and 7·5 per cent. after sixteen days.

The causal mechanism is obscure. It has been variously stated to be due to haemorrhage into the optic nerve-sheaths (von Graefe, 1860); ischaemic fatty degeneration of the optic nerve (Westhoff and Ziegler, 1899); retrobulbar neuritis (Hoffman, 1899); oedema and multiple haemorrhages (Leber, 1877); changed consistency of the blood (Wilbrand and Saenger, 1904); thrombotic foci causing degeneration (Goerlitz, 1920); toxins (Groenouw 1904, Terrien 1921, Kummel 1932, Rønne 1932, Holden 1899, and Duggan 1943). Duggan even identifies the toxin as adrenalin. Langdon (1933) believes that anaemia is the sole factor; Wolff (1935) gives arterial spasm as the cause; Hartmann and Parfonry (1934) blame vaso-constriction; acidosis, ischaemia and the effects of light (Røe,

1942); Cox (1944) thrombosis of the central retinal vein, and Fisher (1929) exudation of fluid into nerve-sheaths. According to Duke-Elder (1940) the mechanism in some ways resembles that of amblyopia due to quinine poisoning.

The main difficulty appears to lie in the fact that it is very seldom that eyes affected are available for detailed pathological examination, and then not at all at the very necessary phases in the evolution of the condition leading up to the fully developed optic atrophy.

There are numerous difficulties besetting all the above explanations, but the major difficulty appears to be to explain the late onset of the condition in so many cases. If severe anoxaemia is the cause, why does it not occur during or immediately after the haemorrhage in all or most cases; why does it so very rarely, if ever, follow massive haemorrhage in the healthy? Some authorities say that blindness never follows a single haemorrhage in a person in normal health. According to Zentmayer (1912) de Wecker, and according to Grout (1914) de Wecker, Kneis, Wilbrand and Saenger did not see a single case in the Franco-Prussian War, where visual disturbance could be attributed to surgical haemorrhage alone. Harbridge (1924) could find only 18 cases recorded in the literature between 1912 and 1924 and including the war of 1914-18. MacRae (1928) says that no instance of this form of sudden blindness was recorded in the 1914-18 war, although Terrien (1921) quotes one case. Goulden (1935) had seen records of two cases. Wolff (1935) quotes Pincus as having seen two cases following amputation.

It is probable that the amblyopia is not due to a single cause, that all the above factors participate in varying degree depending on the underlying local and systemic pathology. However, in view of our knowledge of the changes that occur in the blood after haemorrhage, it would seem that of all these changes, dilution of the blood by tissue-fluids is the one that is most likely to require some hours or even days to occur, and would most closely parallel the onset of the delayed amaurosis. In chronic illness, particularly if it is associated with recurrent small haemorrhages and restricted diet, not only would anaemia occur, but the plasma-proteins and the body-reserve of proteins would be much depleted.

If one of the important features in causing the ischaemic amblyopia to occur were oedema of the optic nerve, this might and could cause some compression of the entering, and even more of the leaving blood-vessels. We would expect this oedema to be more marked in the presence of low plasma-proteins, damage to capillary and vessel walls by ischaemia, acidosis, capillary vaso-dilatation, arteriolar constriction and compression of venules. A vicious

circle would thus ensue. The oedema fluid by compressing the outgoing veins would, if the blood were dilute and anaemic, cause an appreciable fall in the quantity of blood perfusing the retina at any instant. Holden (1899) found after experimental haemorrhage in dogs " changes indicating the presence of a non-coagulable liquid in the nerve fibre layer." Diffuse retinal oedema was also noticed by Goerlitz (1920), and oedema of the optic nerve was held responsible by Leber (1877) and Fisher (1929). Lehane (1941) quotes a case with chronic anaemia, gastro-intestinal in origin, in which transient total blindness lasting three hours occurred suddenly 15 minutes after transfusion had been completed at the rate of 2·0 c.c. per minute. Although he does not believe it is the cause, it is likely that sudden rapid increase in blood-volume above normal with resulting optic nerve oedema may have been the cause here. A similar case of post-transfusion blindness is reported by Jiron (1939).

There would thus seem to be several factors involved, each of which alone is incapable of causing the amblyopia. Anaemia alone does not appear to cause amblyopia, as common clinical experience indicates. Although optic atrophy has been described in pernicious anaemia (Cohen, 1936; Box, 1936; Panton, 1935; Kampmeier and Jones, 1938) it is extremely rare and may perhaps not be related to the anaemia but rather to the underlying sub-acute combined degeneration of the cord. Varying degrees of optic atrophy following retrobulbar neuritis had been noted in chlorosis or iron-deficiency anaemia by a few early authors (Gowers, 1904). Newton (1944) describes a case following anaemia not due to haemorrhage. Amblyopia in the nephrotic syndrome with its low plasma-protein and only mild anaemia must be extraordinarily rare, and we know that amaurosis following a single massive haemorrhage is almost unknown. A fortuitous association of these three factors would thus seem the most likely underlying mechanism. The haemorrhage presumably causes the initial though temporary generalised arteriolar vaso-constriction. The increased capillary permeability thus produced helps the other factors to set the entire cycle in motion.

If we accept the low plasma-proteins in the presence of anaemia as the essential background of the cycle, then we would expect, should the plasma-proteins be very low, sudden onset of blindness simultaneously with a sudden brisk though small haemorrhage. In other anaemic patients, in whom the plasma-protein level is not low, though tissue protein reserves are depleted, we would expect loss of sight to occur not at the time of the haemorrhage but in the post-haemorrhagic state, when the blood-volume is being made up by tissue-fluids, and hence plasma-proteins are being

depleted. Lastly, in fit, healthy, well-fed subjects such as young soldiers, even after severe haemorrhage, anaemia and blood dilution could not occur to the necessary degree causing the required fall in plasma-proteins and yet preserving life. Hence blindness does not arise.

In view of the variety of interest of this condition, two further personal cases are now described. A third case, of which full details are not available, is described in the appendix.

After the description of these two cases, the results of a survey of the literature from January, 1924, until mid-1947 are produced in table form with a brief analysis.

CASE 1.—Mr. C. B., aged 58 years—a farm bailiff—was admitted to hospital with a history of haematemesis 18 hours before admission. On examination, he was a well-covered man in moderately good physical condition; pulse 90 per minute, B.P. 120/60 and haemoglobin 2·7 gms. Apparently he had recurrent attacks of dyspepsia for some years, and a similar attack of bleeding in 1938.

A barium meal at this hospital three weeks after admission showed no evidence of a peptic ulcer. His vision had been bad for some time past, and the fortnight before admission it was definitely getting worse. Two weeks before admission "he walked into a telegraph pole and thought it was the road."

Five days after admission he had a throbbing headache and complained of gradual onset of blindness on the right side. The following day the field of vision of the right eye was restricted to the central part of the temporal field. The right pupil did not react to light. Cranial nerves were otherwise normal. On examination he was very pale, quite orientated, no tachycardia, B.P. 105/65. Heart normal. Urine contained a trace of albumin. Left pupil reacted to light, right pupil was dilated and much larger than left, irregular in outline with a very slight light response. Both fundi showed slight swelling with marked pallor of the discs, the edges of which were indistinct, and faded imperceptibly into the pale retinae. In both eyes the veins were congested and the arteries narrowed and showed a marked light reflex with nipping of veins; there were no exudates and no macular abnormality. Both eyes were presbyopic with limitation of field of vision of the right eye in all directions. But the right eye showed tiny linear haemorrhagic streaks radiating out like a fan from the papilla.

1·35 litres of blood were given by slow continuous drip. Improvement of vision rapidly began and was maintained. The visual field in the right eye increased daily. On discharge six weeks after admission his right eye had improved considerably, but there was still some limitation of the field of vision in all directions. His haemoglobin was 11·5 gm.

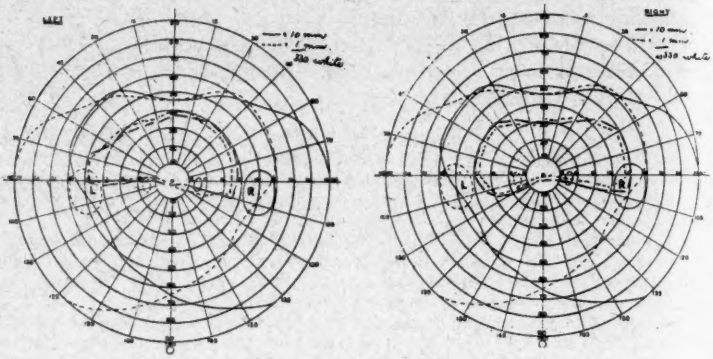
When seen six months later, both discs were rather pale, the right more than the left, but there was no definite evidence of optic atrophy. Vision was normal for him in the left eye, but the right eye had limitation of its field in all directions.

When heard of on August 29, 1947, four years after his first admission to hospital, he was still at full employment as a bailiff. He had no further haemorrhage or dyspepsia. He wrote and informed me that vision in his right eye was slight, but there was no apparent deterioration of the sight of his left eye.

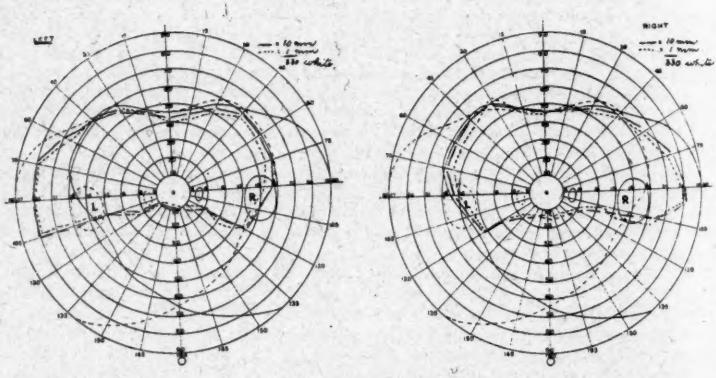
The patient was last seen on December 13, 1947. On that day vision in his right eye was restricted entirely to perception of light in the centre of the field. The right disc was evenly pale and showed a clearly demarcated periphery (optic atrophy). The retina appeared normal except for minimal arterio-sclerotic change in the arteries. There were no exudates or haemorrhages. The left eye showed presbyopic change but a normal fundus oculi.

CASE 2.—Mr. A. G., aged 71 years—a clerk—was first admitted to hospital May 31, 1946, after a road accident. He was discharged August 22, 1946, in a walking-cast, with non-union of his leg fractures. He attended as an out-patient

in the orthopaedic department, and was re-admitted June 26, 1947, with a progressive paraplegia of two weeks' duration. Investigation suggested that this was due to neoplasm. His prostate was large and hard. Formalin-stable serum acid phosphatase was first found to be 2·0 K.A. units. A later figure was 13·0 K.A. units. Treatment was begun with stilboestrol, but in spite of large doses there was no improvement. Laminectomy revealed compression of the cord by secondary growth, probably from the prostate. He developed a urinary infection, and had recurrent



Case II.—Before Transfusion.



Case II.—After Transfusion

attacks of haemorrhagic cystitis which responded to alkalies, fluids and sulphanilamide. In spite of a suprapubic cystotomy this haemorrhagic cystitis recurred. On July 3, 1948, and July 4, 1948, he bled severely from his bladder—this lasted for 24 hours and then ceased. On July 5, 1948, his haemoglobin was returned as 3·7 gm. In the evening of July 5, 1948, he complained of failing vision. On the morning of July 6, 1948, his sight (both eyes) was very poor—he could not read and could just distinguish outlines. He was transfused with two pints of blood on the 6th and 7th July. On the 8th he reported that his vision had improved considerably.

Retinal change at no time was marked. There was only pallor of disc and retina, and 48 hours after transfusion the pale retina became more normal in appearance. However, the discs still looked pale. Except for slight arterio-sclerotic vascular changes, there were no exudates or haemorrhages. On July 13, 1948, his haemoglobin was 7·2 gm. and he could read the large print in the daily newspaper. His blood pressure was 160/80 mm. Hg and his blood urea 41 mgm. per 100 ml.

On July 22, 1948, both fundi appeared normal and he could read small newspaper print, though for short periods only. On August 7, 1948, further vesical bleeding occurred, his haemoglobin was then 4·4 gm., and there was further deterioration of vision. Bleeding ceased in 24 hours and visual recovery began again. Discs now definitely pale. A few hard exudates, arteries very thin; veins congested; no haemorrhages. On August 11, 1948, plasma-protein estimation gave the following result: total protein 4·5 gm./100 ml.; albumin 2·8 gm., and globulin 1·7 gm. Although these proteins are not very low, we feel that during the few days that elapsed after haemorrhage they have been made up from the tissue-protein reserve, as we have endeavoured to maintain this patient on a high protein and high calorie diet. What part bone secondaries play in the blood changes is impossible to assess in this case.

In view of the definite evidence of persistent renal and vesical infection in this case it may be thought that haemorrhage was not the only factor. The low blood-globulin is rather against any marked systemic disturbance of the blood-proteins by the infection. The close relation too between the bouts of prolonged vesical haemorrhage and loss of sight clearly showed that the key mechanism was the haemorrhage, and that at first the process was reversible. This patient later died. No further macroscopical vesical haemorrhage occurred, and no further visual deterioration. However, samples of urine always contained red cells. As we were at no time really able to control his urinary infection, this could not be the cause of the loss of sight, though it was an important accessory factor. The eye was not examined after death, as permission for autopsy could not be obtained.

In this case the main features would appear to be prolonged disability from fractures, paraplegia, carcinoma of the prostate with secondaries in the cord and elsewhere, chronic vesical infection and recurrent vesical haemorrhage. All these features together did not produce loss of sight until profuse bleeding occurred, necessitating transfusion. We feel, therefore, that this can legitimately be considered a case of loss of sight due primarily to haemorrhage.

Discussion

These two cases and the third case described in the appendix illustrate many features common to this condition. The causes are respectively, gastric haemorrhage, vesical haemorrhage and uterine haemorrhage. Out of 106 cases recorded up to 1876 by Fries (quoted by Barr, 1934), 36 per cent. were due to bleeding from the stomach, 25 per cent. due to uterine haemorrhage, and 25 per cent. due to blood-letting. In a survey of the literature from 1924 until the end of 1947 we were able to find 47 cases, including the three in this paper. (See Table.) Where it was possible to ascertain the cause the percentages were as follows: gastric haemorrhage and melaena 47 per cent. (20 cases), uterine haemorrhage 32·5 per cent. (14 cases), nasal haemorrhage 9 per cent. (4 cases) and miscellaneous haemorrhages 11·5 per cent. (5 cases).

Author	Year	Age	Sex	Lesion	Time of Onset (days)	Degree of Recovery of Vision	Source
JONES, F. A.	1947	56	M	Gastric Haem.	8	—	*Brit. Med. J.*, **2**, 477.
		70	M	,, ,,	Immediate	—	*Ibid.* **2**, 477.
BLACK, J.	1945	53	M	Haematemesis and Melaena	—	—	*Ibid.* **2**, 920.
COX, R. A.	1944	22	M	Trauma	?3	—	*Arch. Ophthal.*, **32**, 368.
LONG, A. E.	1943	52	F	Epistaxis	6	—	*Amer. J. Ophthal.*, **26**, 1179.
RØE, O.	1942	66	M	D.U. Melaena	2-3 weeks	Nil	*Acta Ophthal.*, **20**, 48.
TIDY, H. L.	1941	30	F	Post-partum	11	Complete recovery	*Brit. Med. J.*, **1**, 774.
BUSHPAN, A. ...	1941	—	F	Post-partum	—	—	*Vestnik oftal.*, **18**, 325.
ROBERTSON, C. K.	1941	55	M	D.U.	—	—	*Edin. Med. J.*, **48**, 414.
GIQUEAUX, R. E. ...	1941	—	—	—	—	—	*Ann. argent. de oftal.*, **2**, 155..
BAMFORD, C. H. and BARBER, H. ...	1940	46	M	Haematemesis	5	—	*Lancet*, **2**, 715.
MITTELSTRASS, H.	1938	26	F	Post-abor.	—	Partial	*Deutsche med. Wöchenschr.*, **64**, 936
WAUTERS	1938	—	F	Post-abor.	—	—	*Bull. Soc. belge. d'opht.*, **76**, 59.
RUGG-GUNN, A. ...	1938	47	M	Haematemesis	3-4	Nil	*Proc. Roy. Soc. Med.*, **31**, 665.
		23	M	,,	—	Nil	*Ibid.* **31**, 665.
		18	F	Uterine H.	<1 week	Slight	*Ibid.* **31**, 665.
TATARZYNSKA, H.	1938	—	—	—	—	—	*Polska gaz. lek.*, **17**, 338.
DUGGAN, W. F. ...	1936	23	M	Blood Donation	2 weeks	Nil	*Arch. Ophthal.*, **16**, 380.

KORZHENYANTS, S.F.	1935	—	—	—	—	—	*Sovet. vestnik oftal.*, **7**, 391.
HARTMANN, E. and PARFONRY, J. ...	1934	—	—	Melaena	—	Partial	*Bull. Soc d'opht. de Paris.* Feb. 54.
BARR, A. S.	1934	32	F	Post-abor.	Several days	Partial	*Amer. J. Ophthal.*, **17**, 396.
GOLDFEDER, A. E. and *RAPOPORT K. N. (Fuchs case) ...	1934	29	F	Post-part.	Immediate	Recovered	*Klin. Monatsbl. f. Augenheilk.*, **93**, 666.
HARTMANN, E. ...	1933	—	—	—	—	—	*Bull. Soc. d'opht. de Paris.* May, 347.
LANGDON, H. M. ...	1933	39	F	Uterine H.	1 week	Partial	*Arch. Ophthal.*, **10**, 99.
de SCHWEINITZ, G. E.	1933	—	F	Post-abor.	6	Partial	*Ibid.* **10**, 102.
HERMAN, M. ...	1933	—	F	Post-abor.	—	—	*Ibid.* **10**, 102.
LANGERON	1933	64	F	Venesection	Immediate	Nil	*Lyon méd.*, **152**, 176.
WEIL P. E., BOUSSER J. and HALBRON, P. ...	1933	70	M	Nasal haem.	2	Partial	*Bull. et mém. Soc. méd. d. hôp. de Paris*, **49**, 386.
LAPORTE, A. ...	1932	—	—	Haemat.	—	—	*Prat. méd. franç.*, **13**, 727.
GENET, L.	1931	40	F	Miscarriage	10	Nil	*J. de méd. de Lyon*, **12**, 585.
SATANOWSKY, P. ...	1930	22	F	Piles	1	Slight	*Semana méd.*, **2**, 956.
		30	F	Uterine haem.	25	Slight	*Ibid.* **2**, 956.
WHITING, M. ...	1929	40	M	Melaena	—	Nil	*Tr. Ophth. Soc. U.K.*, **49**, 144.
		48	F	Melaena	—	Nil	*Ibid.*
		47	M	Melaena	—	Slight recov.	*Ibid.*
		41	M	Haemat.	3-14	Nil	*Ibid.*
		48	M	Haemat.	7	Nil	*Ibid.*
LISTER, A. E. J. ...	1929	—	F	Uterine H.	2-3 weeks	Complete	*Ibid.*

Author	Year	Age	Sex	Lesion	Time of Onset (days)	Degree of Recovery of Vision	Source
GOULDEN, C. ...	1929	18	M	Melaena	—	Nil	*Tr. Ophth. Soc. U K.*, **49**, 151.
COYON, A., CERISE, CLOG, W.	1927	—	—	Gastro-Intestinal	—	—	*Bull. et. mém. Soc. méd. d. hôp de Paris*, **51**, 53.
GRIMMINGER, W....	1925	38	M	D.U. Melaena	—	—	*Z. f. Aug.*, **57**, 106.
		21	M	Epistaxis	—	—	
HARBRIDGE, O. F....	1924	40	F	Epistaxis	1½	Mod.	*Amer. Jl. Ophthal.*, **7**, 192.
TERRIEN, F	1930	58	F	Haematemesis	9 days	Slight	*La Presse Médicale*, **2**, 954.
LOCKET, S.	1948	58	M	Haematemesis	6	Partial	Present article.
		71	M	Vesical Haem.	1	Partial	
		25	F	Post-abor.	Immediate	Complete	

* These authors quote another case which I have not included in the series in view of considerable doubt. A farmer's wife aged 34 years said to have lost her sight four days after uterine haemorrhage. Transfused with 440 c.c. of blood four months after onset of amaurosis with ophthalmoscopic optic atrophy. Apparently, however, she almost completely recovered and her optic atrophy disappeared. At the time of the transfusion her haemoglobin was 66% and her R.B.C. 4,810,000.

ANALYSIS :

Total No. of cases : 47.

Age Range : 18–71 years.

Site of haemorrhage :

Gastric Haem. and Melaena (Male 15, Female 2)	20
Uterine Haem.	14
Nasal Haem.	4
Misc. Haems.	5

Time of onset of blindness after last haem :

Immediate 4	= 15%
Within first week 15	= 56%
Within second week 5	= 18%
Within third week 2	= 7%
After third week 1	= 4%

Sex Ratio : 20 males to 20 females.

Recovery :

Complete 4	= 14%
Partial 14 (5 only slight recovery)	= 50%
Nil 11	= 36%

Age :

12 under 30 yrs. (7 females)	= 34%
18 under 40 yrs. (11 females)	= 51%
17 over 40 yrs. (13 males)	= 49%
11 over 50 yrs. (7 males)	= 31%

The ages of the three cases were respectively 58 years, 71 years, and 25 years. Terson gives the age range as 2 years to 77 years, but most commonly over 40 years. In the group from 1924 to 1947 the age range was 18 to 71 years. Classically the condition mainly affects males. In our collected survey there were 20 males to 20 females, but in the very small group confined to amblyopia from gastric and duodenal haemorrhage, including melaena, the ratio was 15 males to 2 females. In my own unpublished series of 189 cases of gastric and duodenal haemorrhage the ratio of males to females was 124 to 65. This indicates that in the group of blindness due to gastric haemorrhage males are more likely than females to develop blindness.

The extent of recovery of sight is variable. In the three cases described, one developed almost total blindness in one eye. The second case improved considerably, but he relapsed with further vesical haemorrhage, whereas the third case recovered completely. According to Tidy (1941) in 33 per cent. of all cases there is complete blindness, in 50 per cent. no improvement from maximal loss, 10 per cent. recover good or complete vision, and 7 per cent. show a variable degree of improvement. Singer's statistics were—not improved 45·9 per cent., improved 39·1 per cent., complete recovery 13·5 per cent., recovery with subsequent failure 1·5 per cent. Terson (1922), however, put the figure of permanently blind at 50 per cent. and Pergen (1896) at 54 per cent. Loss of sight is bilateral in 85 per cent. of cases (Duke-Elder, 1940).

The retinae usually show marked pallor and venous congestion. Much less frequently papilloedema, venous stasis and haemorrhages occur (Hurst, 1929), but the retinae may be completely normal without any vision being present. Later the disc becomes increasingly pale, the arteries fine and narrow, and optic atrophy becomes ophthalmoscopically evident. When loss of vision is permanent, it is due to optic atrophy (von Graefe, 1860).

Treatment would seem to be a full diet, including adequate protein intake, in all those chronic diseases in which haemorrhage may occur. Should haemorrhage occur, immediate transfusion of whole blood is advisable. When transfusion has not been available during the early stages, then slow transfusion with packed red cells is indicated.

Summary

(1) The early literature and aetiology of blindness following haemorrhage are briefly surveyed.

(2) Three further cases are described.

(3) An analysis of the cases in the literature from 1924 to 1947 follows.

APPENDIX

Mrs. "X," a young thin woman aged 25 years, was seen while bleeding from an abortion. She was pale and appeared almost exsanguinated. She had evidently been bleeding for some days. Ten minutes earlier she had a severe vaginal haemorrhage, and complained that she was unable to see. Rapid evacuation of her uterus was carried out, and the bleeding ceased. After she had been laid flat on her back with the foot of the bed elevated, she rapidly recovered her sight. In all she was apparently blind for 30 minutes.

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SOME OBSERVATIONS ON THE CAUSATION AND ELIMINATION OF SATTLER'S VEIL*

BY

H. TREISSMAN

LONDON

IN reading this paper, I lay no claim to any new or original theory on the causation of corneal veiling. On the contrary, it is my opinion that there has been too much theorising on this subject and all too little attention paid to the practical side of the subject of fitting with which, I believe, the causes of veiling are inextricably bound up. My aim in this address, therefore, will be to impart my views on the commoner errors in *fitting* which I have found to be constantly present in those cases in which veiling occurs to any appreciable extent. In doing this I shall appear firstly to be departing from the main subject of this paper, namely, corneal veiling; and secondly, to be making an attack on the methods of fitting of certain other practitioners and other types of lenses than moulded lenses. If I convey the latter impression, I offer my apologies in advance and hasten to justify myself on the grounds that, as in all other techniques which aim at precision, there is always a correct and incorrect method of approach.

As a preface to the statements I have to make, I would like to offer some justification for the decided views I hold. I first studied the methods of fitting moulded lenses under Dr. Joseph

* A paper read to the Contact Lens Society on February 21, 1949. Received for publication, March 25, 1949.

Dallos in 1938. At that time it was not unusual to require as many as 20 fittings and 6 to 12 fitting shells before a satisfactory final lens was obtained. Type-glasses were used as the starting point because the use of negocoll and the methods of moulding in those days gave such unsatisfactory results. Naturally, many prospective contact lens practitioners, finding the moulds so unsatisfactory, and not having had systematic instruction in the methods of modifying and fitting moulded shells, preferred to confine their practice to preformed lenses; and around this latter type of lens, a new and (I think) spurious "science" has grown up. I say this advisedly. Innumerable papers have been read and articles written which have absolutely no *practical* value. The mathematics of contact lenses has been delved into and imposing formulae thrust upon the unfortunate student of the subject, who must surely have formed the impression that he will not be able to fit lenses unless he masters these formulae, which is, of course, quite untrue. There have even been tables and slide-rules devised to give the power of contact lens correction which exactly corresponds to a given spectacle correction, to two decimal places; all this in spite of the fact that vertex distance is by no means the only factor in deciding the contact lens equivalent and that only the very best of technicians can work to such fine limits. It is not uncommon to hear or overhear discussion between contact lens practitioners as to the overall dimensions of the lenses they fit, their attention being directed toward a comparison with the dimensions of one colleague's lenses rather than a comparison of the lens with the eye it is meant to fit. All this I mention to show the unfortunate and deplorable tendency to create the spurious and entirely unpractical science to which I have already referred. Throughout the past ten years I have confined my attention to the fitting of moulded lenses and can now claim to be able to fit these lenses in one or two sessions of actual fitting, and to be able to eliminate corneal veiling in my cases. I therefore trust that I shall not be unduly criticised for the expression of decided opinions on this subject.

Among the theories put forward to explain the phenomenon of corneal veiling by contact lenses are that it is due to:

1. Embarrassment of the limbal circulation.
2. Unsuitability of the buffer solution used—(*a*) in its crystalloid content and (*b*) in its pH.
3. Interference with gaseous interchange at the cornea.

The matter of circulatory embarrassment was soon disposed of by providing what was considered adequate limbal clearance. Indeed, in certain quarters, limbal clearance is carried, as a

routine practice, to such an extreme that the bearing area of the scleral portion of the lens is reduced very materially and the optic occupies almost the entire lens. And still veiling occurs. It is hardly surprising, therefore, that the attention of investigators is so steadfastly turned in other directions in an endeavour to solve the problem of misting. It is in this latter departure that, in my view, the mistake lies. Exhaustive research in this country, and by whole teams of investigators in the United States of America, have led only to the conclusion that (1) the pH of the buffer solution undergoes a change towards the acid side by prolonged contact with the cornea (which, incidentally, should never be the case in a well-fitting lens), and (2) that wearers of contact lenses must conduct their own investigations into the optimum solution for their own particular needs. All this is leading exactly nowhere but is serving to make the wearing of contact lenses a subject of ever-increasing burden and complexity, whereas it should, after all these years, have been greatly simplified. The one line of investigation which calls for skill rather than science has been culpably neglected.

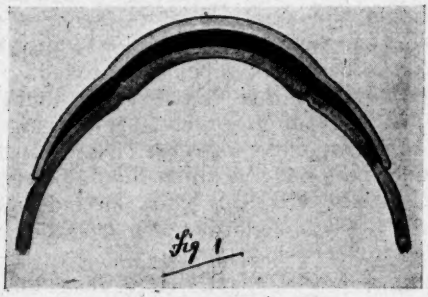
With reference to the rôle played by the buffer solution in causing irritation or veiling, or both, it appears to me to be wasted effort to investigate this matter because, undeniably, in a good contact lens the buffer solution should be entirely replaced by the tears in 15 to 20 minutes. This can be demonstrated quite easily and I shall undertake such a demonstration with pleasure whenever called upon to do so.

If the wearing of a contact lens were to cause misting by interference with gaseous interchange, why is misting not present on waking from sleep or after prolonged unconsciousness? I will not dispute the observation that prolonged contact of buffer solution with the cornea results in its absorption of CO_2 and consequent change in its pH. But, as I have already stated, such prolonged contact is certain evidence that the lens is unfit to be worn.

During the past three years I have made careful examinations in my practice of all lenses which have caused misting, and have compared them with those which were known to give rise to little or no veiling. Each lens was carefully palpated as well as examined *in situ*. Many of my colleagues, when handed a lens, will reach into their pockets for a vernier with which to measure the overall diameter and learn absolutely nothing about the lens except that it is larger or smaller than those he is able to fit. When I am handed a lens, I run my finger over the inner surface of the scleral portion and I derive much useful information about the lens and about the practitioner who fitted it. Every one of

the lenses which caused veiling exhibited one or more of the defects which I am about to describe, and when these defects were, for experimental reasons, only partly corrected, there was a partial improvement as evidenced by the ability to be worn for longer periods without misting and with less discomfort. Further correction of the defect led to further clinical improvement, and finally their complete eradication made trouble-free wear possible for twelve hours or longer. I shall now proceed to an account of the ways in which contact lenses may, in fitting badly, give rise to corneal veiling, and I propose first to touch briefly upon preformed lenses.

The original Zeiss-type lens must, of necessity, have a narrow haptic and consequently a small area of actual contact with the eye. Since the stability of a contact lens depends primarily on



the capillary action of the film of fluid between it and the eye, it follows that a lens with a narrow scleral segment will be relatively unstable in accompanying the movements of the eye. It has therefore been, and still is, the custom to keep these lenses tight at the periphery in order to reduce their mobility (Fig. 1). This has the double effect of creating circulatory obstruction and imprisoning the buffer solution so that the original solution may be retained in the precorneal space for the whole period of wear. Its pH is thus liable to considerable change, due to absorption of CO_2. I am neither supporting nor refuting the suggestion that changes in the pH of the precorneal fluid play any part in veiling, but a stagnant pocket of fluid, in prolonged contact with the cornea, is decidedly unphysiological and is to be avoided, quite apart from the indication it gives of bad fitting.

Now, because of the narrowness of the scleral portion of the Zeiss lens, the method of dry fitting is not easy to apply and

the otherwise less satisfactory fluorescein method must be substituted. I maintain that the fluorescein method, often unreliable, is particularly unreliable at the corneo-scleral junction, and in an effort to avoid fitting a peripherally tight lens and its attendant

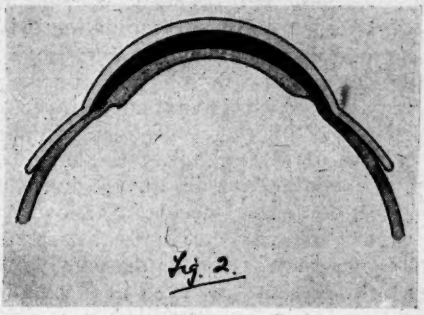


Fig. 2.

consequences, it is a very easy matter to swing to the other extreme and fit a shallow lens (Fig. 2). Clinically the results may be identical with those described above, except that the zone of circulatory embarrassment is moved to the corneo-scleral junction and impairs not so much the circulation itself as the process of

Fig 3

drainage of the corneal fluid into the bloodstream. The effect on the cornea will be much the same and stagnation of the precorneal fluid also occurs. It may be argued that the final limbal clearance given by the technician will eliminate this, but it serves only to move the ring of contact a fraction farther out.

Let us now pass on to consideration of moulded lenses and turn our attention first to a study of the plaster cast obtained from an average good mould (Fig. 3). The corneal portion and a

zone 5 to 8 mm. wide immediately surrounding it will be a fairly accurate representation of the corresponding parts of the eye. But in the vast majority of cases the peripheral part of the cast will show elevations caused by folds of the conjunctiva of the fornices. Even when special measures are taken to avoid such folds, and the resulting cast appears to be free from them, careful inspection under oblique illumination will reveal some elevation at the periphery. There is likewise a very constant narrow elevation immediately around the corneal portion. The almost constant presence of this annular eminence, which has no visible counterpart on the eye itself, is of the first importance in the study of corneal veiling, for it can only be produced by heaping up of the conjunctiva in this region, and it indicates that either by swelling or by mechanical movement of the conjunctiva, or both, there is a noticeable tendency for the conjunctiva to move towards the limbus even in the very short time and very light pressure involved in the taking of a mould. This matter will presently be mentioned more fully. Before the plaster cast is sent to the technician, it should, of course, be modified to remove the elevations and restore continuity with the normal curve of the more central portion of the cast, both in the antero-posterior plane and in the frontal plane, making due allowance for the usual prominence found in the upper temporal quadrant, and for the upper and lower nasal "shoulders" consequent upon the more or less sudden transition from a lesser to a greater steepness of the scleral curve on the nasal side. If modification of the plaster cast is skilfully and adequately carried out, there is no reason why a shell made from it should need more than smoothing on its inner surface to effect successful fitting. The arrival at this happy stage in one or two sessions of fitting should not be the result of a fluke, nor need it provide occasion for celebration. It should and can be a consistent occurrence. The usual failing is to remove too little or none at all of the redundant plaster surface, and then to assume that the resulting shell is ready for finishing.

An inadequately modified plaster cast will yield a shell like that illustrated in Fig. 4. That portion of the shell between A and B or between C and D will follow the contour of the eye, whilst beyond B and D the shell will stand away from the eye. Now, the pressure of the lids on the loose periphery of the shell will cause heavy contact in the accurately fitting circum-corneal zone. We are now faced with two alternatives. If the periphery is very loose, the plaster should be further modified and another shell requested. If, on the other hand, the periphery is not very loose, the correct curve can be extended throughout by grinding

away the more central zone of the shell. This has the double advantage of saving a second shell and of reducing the *corneal* clearance created by the technician when the inner corneal surface was given a uniform radius of curvature. The process of grinding down the inner scleral surface must be carried *right through to the margin of the corneal portion*. Usually this is

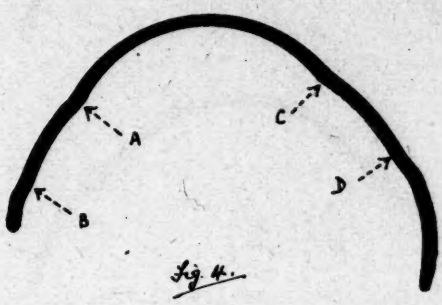


Fig. 4.

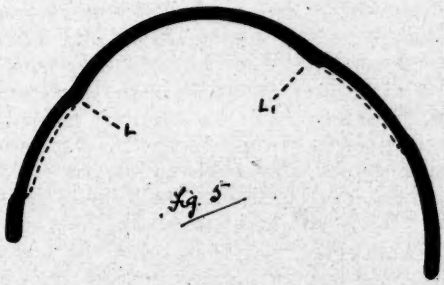


Fig. 5

not done, and the result is that an annular " lip " (Fig. 5, L, L_1) remains so close to the corneo-scleral junction when the lens is *in situ* that no blanching is seen, nor will it be revealed by the use of fluorescein. It can, however, be discovered by passing the finger over the inner surface *from the periphery towards the centre* (a lip can always be felt if the finger is passed in the reverse direction), and by the process of dry fitting. Again, it may be argued that the lip will be removed when the limbal transition is made by the technician, but this is not necessarily so. If the lip is wide, as it might easily be, polishing the limbus will merely move the summit of the lip farther out (compare Figs. 6 and 7).

The effect of retention of this annular lip is, amongst other things, to set up the identical set of circumstances already

Fig. 6

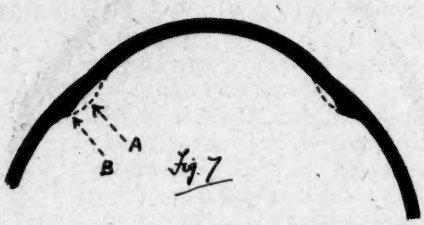
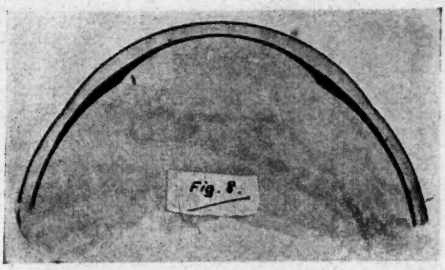


Fig. 7

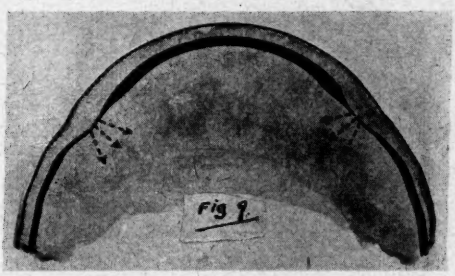
described in connection with preformed lenses, namely, circulatory embarrassment and stagnation of the precorneal fluid. Compare Figs. 8 and 9. With a well-fitting lens there should be capillary clearance over the whole of the surface (except where there is limbal clearance), and the capillary film of fluid should be in a constant process of replacement by the tears, so that the physico-chemical relationship between the cornea and the precorneal fluid is as near the normal as it could possibly be with a lens *in situ*. If, on the other hand, the lens has a "lip," as in Fig. 9, the first effect will be to cause the lens to stand off, and capillary clearance no longer exists anywhere. Later, pressure of the lids causes indentation of the eyeball, circulatory obstruction and closure of the precorneal space, so that the precorneal fluid stagnates. So consistently have I found this set of circumstances when veiling was present that, for ease of reference, I would like to name it. I would like to call it **"choked cornea."** The term is hardly less scientific than "choked disc," and I feel that the two conditions are not entirely dissimilar in their pathology despite their different aetiology.

There is yet another way in which "choked cornea" may be induced, even when no annular lip is present. Let us suppose that a lens has been completed which fits the eye perfectly, and in which there is limbal clearance which, at the time of final fitting, is considered adequate. And let us suppose also that the patient's conjunctiva is thick (as often happens) and tends to swell

readily with every stimulus. We have already seen that the mere insertion of the moulding shell into the conjunctival sac causes slight heaping-up of the conjunctiva around the cornea. Whether this is the mechanical shifting due to the very slight pressure involved, or due to swelling in reaction to the foreign body, is

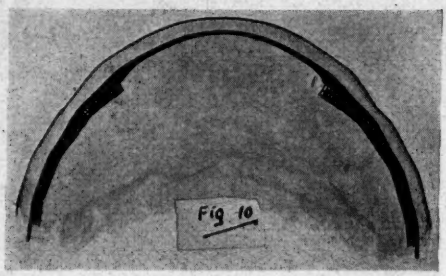


immaterial, because both these factors are present when the lens is worn. But if these factors, operating for several minutes, can cause sufficient heaping of the conjunctiva in this situation to be seen easily on the mould and plaster cast, how much more so will it occur after one or two hours of heavier pressure? The important point is that the conjunctiva *does* swell very con-

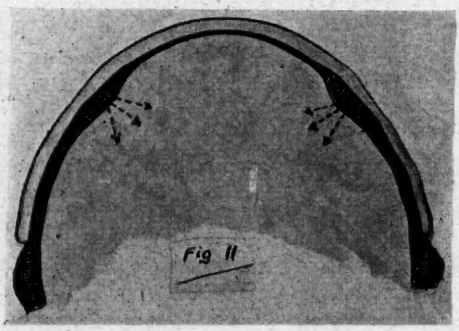


siderably in many patients after a period of wear which varies with the individual case. It first becomes compressed against the scleral part of the lens, cutting off circulation of the tears through the precorneal space. It then spreads outwards and inwards, the latter movement filling up the limbal clearance and, probably, raising the pressure in the precorneal fluid. Later still, pressure of the conjunctiva on the globe will embarrass

the limbal clearance (compare Figs. 9 and 11). So once again we find all the requirements for the inducement of choked cornea. This will not be discovered unless the wearer is seen when the lenses are being worn and have been worn for a sufficient length of time to set up these conditions. It will not be readily discovered



even then unless the lens is lifted carefully from its seat without actually removing it from the eye. To remove the lens straight away in order to re-insert it with fluorescein will mean the loss of all the evidence. If the wearer attends without having worn the lenses for the time requisite to set up misting, and the



lenses are inserted at the time of examination, nothing at all will be found to account for the veiling, and the practitioner's attention will once again be directed towards consideration of the suitability of the buffer solution. The unfortunate patient will be sent away with yet another bottle of buffer solution to start the process of self-investigation *de novo*. Or recourse may be had to fenestration

as an easy way out of the difficulty. What an admission of bewilderment and failure this is!

It is my firm conviction that the set of circumstances to which I have referred as "choked cornea" is primarily responsible for setting up corneal veiling, and that the varying degrees of severity experienced are dependent on whether one or more defects are present in any given case. My conclusions may be summarised as follows:

Corneal misting is due to:

(*a*) Annular pressure on the globe by a "lip" or by excessive swelling of the conjunctiva.

(*b*) Stagnation of the precorneal fluid, especially when there is excessive corneal clearance.

When (*a*) is present, (*b*) is present also, and the result is veiling and intolerance.

(*c*) Excessive corneal clearance alone, *i.e.*, in the absence of any other defect, may cause veiling without discomfort because complete replacement of the precorneal fluid by the tears is a much slower process than when a capillary film of fluid is present. The fluid is thus exposed to absorption of CO_2 to a greater extent than would otherwise be the case.

This paper would not be complete without some reference to fenestration. I have no personal experience of fenestration in my cases because I have not had to resort to it. But I have, on many occasions, discussed it with colleagues, and have examined patients wearing fenestrated lenses. It would appear that in the early days of fenestration this procedure was applied to cases of severe and early veiling and, as is the case with all new and spectacular measures, the results were so startling that it was soon adopted by many as a routine practice. It is not surprising that such a simple method of overcoming the most difficult problem which besets contact lens fitters should soon become universally adopted. It served, however, more than any other single factor, to divert attention from the main subject of fitting, for if fenestration eliminates both veiling and discomfort, what else matters very much? This was followed by a fallacious line of reasoning. If one fenestration is good, two must be twice as good. And before very long we were to see or read of lenses with as many as twelve fenestrations, and what began as a contact lens ended by looking something like the top of a sugar castor. It was even stated that the tears would enter the precorneal space through certain openings and leave it *via* others. All that appeared to be missing were the sign posts which would ensure that the tears would follow the prescribed route! Such is

the nonsense which has been spoken, written and practised in the sphere of contact lens fitting. Obviously, when conditions illustrated in Figs. 9 and 11 exist, the drilling of a hole at the limbus will relieve the stagnation of the precorneal fluid and a certain amount of the circulatory embarrassment. Two or more holes will relieve the circulatory obstruction more effectively. But fenestration does not eradicate the underlying defects; on the contrary it diverts all attention from them and, in addition, introduces other evils hardly less distressing to the wearer than the misting. Add to all this the reluctant admission that fenestration does not always entirely eliminate veiling and we have all the data necessary to assess its true value. I now feel entirely justified in my persistent refusal to introduce this measure into my practice.

I will end this paper with a plea for more rationalism. Contact lens fitting primarily is an art and to a much less extent a science. To obtain, as nearly as possible, uniformly satisfactory results, one must fit lenses as *large as possible* consistent with free movement of the eye and this means moulded lenses, with capillary clearance *everywhere* except for adequate limbal clearance. This cannot be learned even from the finest text-books, but calls for patience and training under good supervision. There's the rub. So many prospective practitioners cannot, for economic or other reasons, take the necessary instruction, not realising that, once mastered, the technique of fitting this type of lens is so simple and satisfactory that they would not subsequently fit any other type. But it is so much easier, at first, to fit preformed lenses by following written instructions in a book, and the results are at least as good as those obtained with " moulded " lenses as fitted by the uninstructed. So we find that almost all contact lenses nowadays are either the Zeiss type (these are, surprisingly enough, still being supplied to patients !) or unsatisfactorily fitting " moulded " lenses, or the hybrid " modified " preformed lenses. Learned papers are read which are of academic value only, and a spurious science is growing up which is leading exactly nowhere. The reputation of contact lenses is, so far as the wearing public is concerned, rapidly going downhill, as it appears already to have done in the U.S.A., where all these unfortunate tendencies have been further complicated by the inherent dislike of any procedure calling for individual attention, and where the urge to mass-produce has given rise to the cone lens, the special curve lens and now the corneal lens. All these have had or will have their day, until it will no longer be possible to sustain the extravagant claims made for them. Only the properly fitted moulded lens will continue to give comfortable trouble-free wear and to maintain its well-earned reputation. It has been argued that these

lenses are too expensive to be available to the mass of prospective wearers and that some less expensive lens is needed. This argument is raised in support of the makeshift lenses which I condemn. My reply is that these lenses are no less expensive, either because their cost cannot or *will* not be reduced. It appears to me that the only way of making satisfactory moulded lenses available at the minimum cost is to have as many practitioners as possible who are trained to fit these in the minimum number of sessions of actual fitting. One could not hope to mass-produce dentures in order to reduce their cost. Why should we expect to achieve this in the realm of contact lens work?

Summary

Corneal veiling must not be treated as an isolated symptom but is inevitably bound up with the subject of fitting. It is due to defects in fitting which give rise to circulatory obstruction of varying degrees of severity, or to stagnation of the precorneal fluid, or to both. Stagnation of the precorneal fluid alone will give rise to slight veiling without intolerance, the veiling being usually only noticed in artificial light. When combined with circulatory embarrassment, veiling is more severe and is accompanied by irritability and intolerance. The remedy lies in correcting or avoiding the defects, not in relieving their consequences by drilling holes in the lens. All the untoward symptoms associated with contact lenses, veiling included, can be avoided by bringing the practice of fitting out of the academic and theoretical clouds down to solid earth.

A PRELIMINARY NOTE ON A NEW METHOD OF FIXING CORNEAL GRAFTS

BY

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I DID not intend to publish this small work until I had sufficient cases to demonstrate its usefulness or otherwise. With the present lack of donor grafting material in New Zealand, however, opportunity for these operations is infrequent; and as the method appeared so successful in the cases I have done, I decided to make this preliminary note.

In 1941 this method first occurred to me while considering the

technique of keratoplasty in general. It seemed to me that it would often be an advantage to have a fairly big graft (5 to 6 mm.). To get consistently good results and avoid anterior synechiae, one would have to aim at a water-tight joint. The ideal would appear to be perfectly clean-cut corneal discs of equal size from the donor and recipient, with no attempt at bevelling. If this were possible, the graft would fit like a plug, and would tend to be thrust out by the re-forming aqueous under intra-ocular pressure. There would be no tendency for it to go into the anterior chamber unless there was escape of aqueous allowing it to tilt. For these ideals a circular graft would theoretically be preferable to a square one.

This ideal would obviously be difficult to attain, and there would often be irregularities, at least in the deeper portion of the recipient cornea. Thus there would not always be a perfect fit, and so the aqueous would tend to leak. If the fit were perfect, the ordinary criss-cross sutures would hold the graft satisfactorily, and there would be no leak. With suture fixation, however, there would be nothing to prevent a leak at any irregular or weak point.

How then to improve on the existing methods of fixation in preventing aqueous leakage? The simplest method seemed to be to have something to cover the whole wound, slightly overlapping the cornea on each side and firmly fixed to the eye-ball. Some non-irritant metal unaffected by body fluids seemed most suitable. The idea was to have a ring made out of thin sheet metal 1·5 mm. wide, of such a circumference as to overlap the trephine cut by 0·75 mm. on each side, and with four arms 1·5 mm. wide to reach just beyond the limbus with notches cut near the ends of the arms for sutures tied round them to grip. The whole was to conform to the curvature of the cornea, the ends of the arms altering their curvature slightly as they came on to the sclera, where they were to be sutured, thus avoiding all sutures in the cornea.

My first experimental " corneal splint " was made of platinum. I made a cast of a rabbit's eye to which a thin sheet of platinum was moulded, and from which the splint was then cut. I experimented with dead rabbits' eyes, comparing this fixation with the various suture methods, and increasing the intra-ocular pressure by injecting saline. I also tried using egg-membrane between the cornea and splint as an extra seal against leakage, but the splint alone seemed to give sufficient closure. I was then preparing to do some research with live rabbits, but this was prevented by my being moved to another naval station, and I was unable to do any more until after the war. Then return to

civilian practice left little time for research, but eventually, after some further experimenting, I devised the present splints and trephine guides, which I shall describe.

FIG. 1.

Top. Guide and Splint used in Case No. 2 (Corneal surface)
Lower. Guide and Splint used in Case No. 3. (Outer surface)

I have modified my original *splint*, shortening the arms so that they end over the cornea near the limbus. This is preferable to carrying them on to the sclera because

(1) Corneae vary in diameter, and also in length of different axes.

(2) It simplifies the making of the splint accurately, and leads to a better fit.

(3) There seems no contra-indication to placing sutures in the cornea well away from the wound, and in my experience they are more easily and more accurately placed than in the sclera with overlying conjunctiva.

Then there is the *trephine guide*, which is an essential in this method. It is an exact replica of the splint, except that the central aperture is enlarged so that it will just permit the entry of the trephine.

At operation the guide is first placed on the cornea. Then while it is held there, a suture is placed in the cornea beneath the end of each arm of the guide. These four sutures are tied once without completing the knot. This will hold the guide firmly in place. The trephine is then placed in the aperture in the guide

and a cut made—perhaps one-third of the way through the cornea. It is then removed, and the guide also removed after loosening but not undoing the suture-loops. The trephining is then completed in the usual manner. When the graft is put in place the splint is immediately applied, and the sutures tightened over the arms and the knots completed. We know that the splint will exactly cover the trephine cut with an equal overlap on each side without having to fit or measure it, because of the calculated association of the dimensions of the guide and splint.

The present splints and guides are made of platinized gold, and are of a thickness of 0·2 mm.

The pair used in case No. 2 were for a 4·5 mm. graft and of the following dimensions:

Splint—Internal diameter	= 3	mm.
External diameter	= 6	mm.
Overall diameter (end of arm to end of arm)	= 10	mm.
Guide—As above except that internal diameter	= 4·75	mm.

As there was no apparent unfavourable reaction to the foreign body (splint), and the patient felt no discomfort whatever, it seemed to me that it would not matter if a larger area of cornea were covered by a broader splint. Thus one could make a universal splint instead of having to have separate ones for each size of graft. With the guides it might be best to have separate ones for each size of trephine, or else one could possibly use a guide for the largest trephine, and use collars to centre smaller trephines.

For case No. 3 the following splint and guide were used:—

Splint—Internal diameter	= 3·5	mm.
External diameter	= 8·5	mm.
Overall diameter (end of arm to end of arm)	= 11·5	mm.
Guide—As above except that internal diameter	= 5·5	mm.

It will be seen that the above splint could be used for grafts between 5 and 7 mm. diameter, allowing a minimum overlap on the graft at one end of the recipient cornea, at the other of 0·75 mm.

Notes on Three Cases of Corneal Graft

I have only done three cases between December, 1947 and November, 1948, but they will serve to illustrate some points I have observed. In the first case I used sutures as described by Katzin (1947), and in the last two cases I used my corneal splint.

The first case gave me some anxiety, as he formed an anterior synechia. This,

however, I was able to free on the 18th day after the keratoplasty with a discission needle entered at the limbus without opening the wound. The graft did not become vascularised, but was slightly hazy from epithelial bedewing. The tension, however, was not appreciably raised to fingers—certainly not enough to account for bedewing as usually seen. Therefore I did not suspect glaucoma at

FIG. 2.

Case No. 1. Fifteen months after operation. Photograph poor, as it distorts the cornea and shows image of camera in centre of graft. Actually vision is 6/12 to 6/9 and Jaeger 1.

first but eventually I took the tension with a Schiötz tonometer, and found it to be slightly though definitely raised (30 mm. of Hg. as compared with 17 mm. in the other eye). I did a corneo-scleral trephine after which the cornea cleared completely, and the patient now has 6/12 to 6/9 vision with correction. It would seem from this that a corneal graft may be liable to develop epithelial bedewing at a considerably lower intra-ocular pressure than would a normal cornea.

FIG. 3.

Case No. 2. A, Before operation, showing dense leucoma; and B, one month after operation, showing clear 4.5 mm. graft.

The last two cases in which corneal splints were used have been uneventful, with excellent healing and quick re-formation of the anterior chamber. The third case was a 5 mm. disc, and after the trephine the iris contracted abnormally, so that the whole pupil and much of the iris lay within the trephine circle, but no anterior synechiae formed. That suggests quick reformation of the anterior chamber with no appreciable leak.

FIG. 4.

Case No. 3. One month after operation, showing clear 5 mm. graft. Note white marks near limbus indicating site of sutures that held splint in place.

Pain was absent, and there appeared to be no reaction to the splint in either case, nor was there any feeling of discomfort. In both cases the splints, when they were removed on the 7th day, were found covered by a film of mucus (a similar film was observed on the sutures in the first case) and there was no mark or indication as to where they had been touching the cornea. Therefore in future I think I shall be inclined to leave the splint on longer (ten days or more).

CONCLUSION

It seems to me that the following are the advantages of this method over other methods of fixing a corneal graft such as sutures, conjunctival flaps, etc.:—

(1) A more perfect sealing of the wound, together with prevention of tilting of graft.

(2) Prevention of sudden loss of anterior chamber after it has re-formed.

(3) Greater accuracy and even distribution of pressure over the whole wound.

(4) Simpler technique with assured perfect placing. The criss-cross sutures are quite difficult to place accurately so that they all cross in the centre and spread the pressure equally round the circumference of the graft.

(5) Nothing touches the central area of the graft, which is thus safe from possible injury, and a clear view is left of most of the graft and of the anterior chamber.

(6) I think it will be found that such strict rest for so long after the operation will not be necessary. With experience of more cases, I feel sure I shall be able to relax the restrictions with this method of fixation.

(7) It is appreciated that some cases for corneal grafting will have considerable astigmatism or flattening of the cornea, and it might be thought that this would militate against a good fit of the corneal splint. In reality this is not so, because when the four sutures are tied to the arms, the cornea is more or less made to conform to the natural corneal curve of the splint. In the third case some corneal astigmatism was actually observed, but that did not in any way interfere with the technique. If high astigmatism were encountered, the splint could be slightly bent to conform thereto.

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FURTHER INVESTIGATIONS ON THE ACTION OF DETERGENTS ON THE EYE*†

BY

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INTRODUCTION

It is well known that the incorporation of wetting agents in drug solutions for local application enhances the penetration of the drug into the tissues (McKee *et al.*, 1943; Bellows and Gutman, 1943; Trim and Alexander, 1946). Ginsburg and Robson (1945) have shown that when dodecyl sodium sulphate is incorporated in solutions of sodium sulphacetamide applied to the cornea, the increase in penetration is due to an action of the detergent on the corneal epithelium. The action of the detergents on the eye has been further investigated and the results are described in the present communication.

METHODS

Penetration of drugs into the eye and the isolated cornea.

The methods used have been previously described by Robson and Tebrich (1943) and Ginsburg and Robson (1945).

Drop size measurements. There is a linear relationship between drop size and the surface tension of a solution provided that the age of the surface is constant (Gaddum, 1931). The size of drops formed at a water/paraffin interface was measured as follows: Ten drops of the solutions were delivered from a 5 ml. micro-burette with the tip immersed 1 cm. below the surface of liquid paraffin B.P. in a large crystallising dish. The total volume of solution delivered was too small to alter appreciably the level of paraffin in the dish so that the drops were formed under a practically constant head of paraffin. The time for delivery of ten drops was adjusted to 200 secs. and the volume of the drops delivered was measured.

Chemical Methods. Sulphacetamide was extracted from the tissues by the method of Bellows and Chinn (1939) and was estimated by the method of Bratton and Marshall (1940).

All experiments were performed on mature rabbits of both sexes and various breeds.

RESULTS

Table I shows the results of 36 experiments on the effect of five wetting agents on the penetration of sodium sulphacetamide into the cornea. In the experiments on the isolated cornea the drug was

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applied for 15 minutes, while in those on the intact animal it was applied for 6 minutes. The results clearly show that dodecyl sodium sulphate is the most effective of the detergents tested in increasing the penetration of the sulphonamide both into the living eye and into the isolated cornea. Thus 0·25 per cent. lissapol N increases penetration by 75 per cent., while 0·1 per cent. dodecyl

TABLE I

The effect of different concentrations of wetting agents on the penetration of 10 per cent. sodium sulphacetamide into and through the cornea.

Wetting Agent	Concentration gms. per cent.	Experiment	No. of Experiments	Conc. of Sulphacetamide mg. per cent.			
				Cornea		Anterior Fluid	
				+ W.A.	Control	+ W.A.	Control
Dodecyl sodium sulphate	0·1	Isolated cornea	3	803	357	29·5	8·3
,,	0·5	,,	2	1300	342	38·7	8·3
,,	1·0	,,	2	1915	315	54·4	6·9
,,	0·1	In vivo	6	349	191	29·1	6·4
,,	1·0	,,	1	860	200	77·2	16·1
Ammonium Lorol	1.0	Isolated cornea	2	886	478	17·6	8·9
Aerosol OT	0·1	Isolated cornea	1	434	—	6·9	—
,,	0·2	,,	1	451	449	8·5	7·6
,,	1·0	,,	3	398	365	10·2	11·6
,,	1·0	In vivo	4	389	108	32·3	8·0
Lissapol N	0·1	Isolated cornea	1	430	372	4·1	3·7
,,	0·25	,,	1	603	346	10·3	4·0
,,	0·5	,,	2	850	366	7·3	5·0
,,	1·0	,,	2	1050	295	19·8	4·7
,,	0·1	In vivo	1	114	186	4·2	8·7
,,	1·0	,,	1	601	155	84·9	13·3
C. 60799	1·0	Isolated cornea	2	288	323	2·3	2·6
,,	1·0	In vivo	1	48.8	61·9	3·3	5·5

sodium sulphate increases penetration by 125 per cent. C 60799 has no effect on the penetration of the drug. According to Bellows and Gutman (1943) aerosol OT is highly effective. In the present experiments it had no effect on the isolated cornea, but in the intact eye 1 per cent. of aerosol OT increased the penetration by 260 per cent. compared with 330 per cent. for 1 per cent. dodecyl sodium sulphate and 288 per cent. for 1 per cent. lissapol N.

Table II shows the penetration of sodium sulphacetamide with

aerosol OT into the eyes of anaesthetised rabbits and under the same conditions into the eyes of dead and cold rabbits.

In the living animal, aerosol OT increases the penetration of the drug, but has no effect when applied to the dead animal. The

TABLE II

The penetration of sodium sulphacetamide with aerosol OT into the eyes of living and dead rabbits.

Tissue	Mg./100 gm. sulphacetamide			
	Living		Dead	
	S	S + A	S	S + A
Conjunctiva	135	416	704	568
Aqueous	8·0	32·3	3·5	4·3
Cornea	108	387	100	148
Iris	11·0	38·9	9·9	16·9
Sclera	42·0	100	42·1	30·2

The figures are the mean of 4 experiments.
S — 10% sodium sulphacetamide.
S + A — 10% sodium sulphacetamide plus 1% aerosol OT.

difference in the action of aerosol OT in the living and dead animals may be due to differences in temperature.

Two of the wetting agents, lissapol N and C 60799 (supplied by I.C.I), are non-ionic and therefore form stable solutions in the

TABLE III

The effect of age of solution on the action on the isolated cornea of lissapol N. and dodecyl sodium sulphate.

Detergent, etc.	Sulphacetamide concentration in Cornea Mg./100 gm.	
	24 hr. old solution	Fresh solution
Lissapol N. 0.5%	668	696
Dodecyl sodium sulphate 0.5% ...	653	1240
None	—	334*

* The figures are the results of one experiment except the control which is the mean of 21 experiments.

presence of high concentrations of sodium sulphacetamide, while the ionic detergents coagulate within an hour after the preparation of the solutions. The results on Table III show that 24 hours after the preparation of the solution the activity on the isolated cornea of dodecyl sodium sulphate is halved while that of lissapol N is unimpaired.

In Table IV the effect of the wetting agents on the interfacial tension at a water/paraffin interface is compared with their effect in increasing the penetration of sulphacetamide into the isolated cornea. It will be seen that the order of the effect of the detergents on the interfacial tension is aerosol, lissapol, dodecyl sodium

TABLE IV

Effect of wetting agents on the interfacial tension at a water/paraffin interface and the percentage increase in the absorption by the cornea of 10 per cent. sodium sulphacetamide.

Wetting Agent	Percentage increases in absorption by cornea	IT. Water/Paraffin Vol. of 10 drops
NIL	0	1·79
Lissapol N 0·1%	14	0·095
,, 0·25%	74	0·071
,, 0·5%	170	0·063
,, 1·0%	290	0·060
Dodecyl Sodium Sulphate 0·1% ...	125	0·148
,, ,, 0·25% ...	—	0·138
,, ,, 0·5% ...	300	0 149
,, ,, 1·0% ...	510	0·144
Aerosol OT 1.0%	10	0·044

sulphate, *i.e.*, the reverse of their effects on sulphacetamide penetration. The interfacial tension of detergent plus drug solutions is not lower than the interfacial tension of solutions of the detergent alone, suggesting that in the concentrations used in these experiments, there is no tendency for complex formation between drug and detergent at the interface.

Effects of detergents on the living cornea.

A mucoid discharge on the surface of the cornea was observed when detergents were applied in concentrations, which increased penetration by 200 per cent. or more. After the application of 0·1 per cent. dodecyl sodium sulphate for 15 minutes *in vivo* the cornea stained with fluorescein, showing that the epithelium over the whole surface of the cornea had been damaged. Examination of eyes with the slit-lamp after six hourly application of drops of detergent solutions, showed oedema of the epithelium and punctate staining of the cornea with fluorescein confined to the anterior surface. These changes were more marked with 1 per cent. than with 0·1 per cent. dodecyl sodium sulphate. One per cent. lissapol N given in the same way produced a slight discharge and very

slight conjunctival oedema, these effects disappearing in 24 hours. Two successive hourly applications of drops of 0·5 per cent. lissapol N produced no abnormalities.

Discussion

The application of drugs with detergents to the eye enables the drug to penetrate the corneal epithelium and hence therapeutic concentrations may be established more rapidly and maintained for longer periods in the posterior layers of the cornea and in the anterior chamber. Of the detergents tested, dodecyl sodium sulphate is the most effective, but lissapol N has the advantage that it forms stable solutions in the presence of high concentrations of sodium sulphacetamide.

Trim and Alexander (1946) have shown that the effect of detergents in increasing the penetration of hexyl resorcinol into ascaris is due to the formation of a complex between the drug and the detergents, and that the order of effectiveness of detergents is the same as for their effect in lowering the interfacial tension at paraffin/water interfaces. In the present work, no evidence of compound formation between the detergents and sodium sulphacetamide was found, and the order of effectiveness of detergents in increasing the penetration of sodium sulphacetamide into the cornea is the reverse of their order for the lowering of the interfacial tension at paraffin/water interfaces.

The detergent increases the penetration of sodium sulphacetamide into the cornea by an effect on the corneal epithelium, possibly by solubilising the intercellular cement. After the prolonged application of detergents the epithelial cells may become completely dispersed. Detergents should not therefore be applied to the cornea for long periods and in high concentrations, and where the epithelium is damaged they offer no advantages as they only increase penetration through an undamaged epithelium.

Summary

The effect of five detergents on the penetration of sodium sulphacetamide into the eye was investigated. Sodium dodecyl sulphate was found to be the most effective.

There is no relation between this action of the detergents and their effect on the interfacial tension at a water/paraffin interface.

Effects of detergents on the cornea are described limiting their possible clinical uses, which are discussed.

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THE ARTIFICIALLY PRODUCED RETINAL PULSE

BY

N. PINES

LONDON

IT is a well-known phenomenon that if the disc and its neighbourhood are observed while external presure is applied on any part of the globe, at a given moment the arteries in the disc start to pulsate. The artery empties and blanches corresponding to diastole, and fills up with blood corresponding to systole, or as Duke-Elder well puts it: "The blood column flashes across the disc." It is possible by greatly increased pressure to abolish completely the pulsation of the arteries on the disc—a procedure very unpleasant to the patient and rather dangerous. The veins on the disc are behaving in a peculiar way. When the first arterial pulsations appear on the disc, the venous pulse is accentuated, but usually does not change its character. With increased pressure on the eye, just before the arterial pulsation is completely abolished, the veins gradually become narrower, exhibit first a trickle of blood and then this trickle becomes beaded; finally the vein blanches completely. This is a summary of the general description of the artificially-produced arterial retinal pulse as given by such distinguished authorities as Baillart and Duke-Elder.

Some important details may now be added. Baillart (p. 28, ed., 1923) wrote that normally the retinal arteries look immobile. He mentions the opinions of Kummel and of Dr. Steyer, that they personally saw the pulsation of the light reflex (the retinal pulse), but not that of the central artery. I described some years ago that in red-free light one can easily see the pulse wave in nearly all primary and in some secondary branches of the central artery in a normal person, if the waves formed by those branches

are sufficiently prominent. The same applies to the rare but beautiful cases, where a primary branch of the artery forms a partial ring on the disc. This kind of pulse is easily explained by haemodynamics, and will not be considered in this paper. But if one applies very gradual pressure to the globe, one will first see a peculiar trembling of the arteries, difficult to describe, but very beautiful to behold. This trembling will be rhythmically intermittent and will correspond to the pulse wave. This is the moment, in my opinion, when the applied pressure plus the intra-ocular tension will be equal to the diastolic pressure of the central artery. The wall of the central artery will be unsupported; the diastolic pressure from inside will be equal to that from the outside, and the wall will contain that additional stimulus to extra contraction that is usually brought on by increased internal pressure, *i.e.*, this trembling is due to the vibration of the wall of the artery under the impact of the systolic wave. Let us increase our pressure a little, and the artery will start to collapse. This will start first deep in the disc on the proximal part of the primary branches, and it will spread to the periphery of the disc only with further increase of the pressure. The veins will become slightly narrowed, but their pulse will be accentuated. This is the level of the mean pressure. Baillart thinks that this is the level of the diastolic pressure, and that what we see is the vibration of the wall of the vessels. In my opinion we see the actual collapse of the artery.

Let us now increase the pressure still more, and watch the disc very closely. This flashing column of blood will reach the periphery of the disc and will be seen in the primary branches as well, not far from the disc, but with one great difference—the arteries on the disc are empty and, during the diastole, collapsed, to fill up in the systole; the same arteries on the retina will never collapse, although the arrival of the systolic wave can be actually seen. Why should it be so?

It is thus a strange fact that one can never collapse the retinal arteries, starting from outside the disc, even if the pressure is much higher than the systolic, and that the arteries on the disc will be completely empty and all pulsation will cease. These facts are not mentioned or described by anyone, except Baillart. He is emphatic about this—p. 39—" Cette observation (des vaisseaux) doit porter sur les artères sur le disc de la papille et non au delà." On page 51 he returns to that, and tries to explain it *en passant* " nous avons vus que les artères retiniennes ne battant que sur le disque papillaire; cela tient sans doute à ce qu'au delà du nerf optique elles sont incluses dans la tissue retinienne. . . . Quoi qu'en soit. . . . "

There is a definite law of hydraulics, that if pressure from outside is applied on any part of a ball full of liquid, inside this ball the presure will be equal in all directions. The eye is such a ball, with a not very elastic outside membrane—the sclera—with a scarcely compressible vitreous gel. Therefore the retina and the vessels will be under equal pressure everywhere, *mutatis mutandis*. Is the turgor of this tiny and fragile membrane such that, caught between the sclera and vitreous, even with the cushion effect of the uvea behind it, it will be able to stand *per se* a pressure higher than the systolic retinal pressure, even though the blood-vessels run only in one or two layers of the retina? It is hardly conceivable, however, and it is contradicted by the fact that the patient will notice a darkening of the field of vision—the best proof that the circulation is at a standstill. The possible explanation of this strange inability of the observer to collapse the retinal arteries, so much narrower on the retina than on the disc—and there they are collapsed—might be looked for, in my opinion, in a different direction.

If the pressure inside the eye is equal, then why should the collapse of the artery be seen first in the centre of the disc, not simultaneously on the whole of the disc? Because here the vessels are nearest to the acute angle formed by them on the disc. The greatest vascular obstacle to the pulse-wave will be this 90° angle —this is why we see normally the pulsation of the vessels on the retina if the waves are sufficiently prominent—and what we observe is the stoppage of the pulse in the main artery of the optic nerve, when the pulse-wave has to overcome the difficulty of penetrating the arteries on the disc passing through this acute angle.

If my reasoning is correct, then what we measure is not the diastolic pressure of the central artery at all, but that of the ophthalmic artery. So thinks also Duke-Elder (Vol. I, p. 707). Let us now see what is going on under the cuff of the sphygmomanometer when applied on the brachial artery. When inflation of the cuff is started the air, as is usual with gases, will try to form a kind of round ball in the middle of the rubber, and from then will spread gradually to the sides, so that the artery will be first compressed in the middle, and from then to its extremities up and down, leaving some small corners at the upper end, where the artery will not be completely compressed. Even before the level of the diastolic pressure is reached in the cuff (say 70 or 80 mm. of mercury) the venous pressure (17 cm. of water) will be overcome. Sainsbury argued (on proper theoretical grounds, that the colloids are incompressible and blood is a colloidal mixture), that really the artery under the cuff remains permanently patent.

It would be so, if the blood from the artery could not escape. But it does, and it goes not back toward the heart, but forwards to the periphery. The artery does therefore completely collapse, as it is seen to be doing on the disc in the eye. The venous stasis therefore starts in the arm before the level of the diastolic pressure is reached. With increased pressure in the cuff a stream of blood will reach the brachial artery from the subclavian, and an increased outflow from the brachial artery will go towards the periphery. It will be accommodated by opening up more capillaries in the periphery and their increased effort to expel the extra blood into the venous system. The veins will swell more, the cyanosis of the lower portion of the arm up to the lower edge of the cuff will increase, and the venous pressure will rise enormously and quickly, being nearly equal to the systolic pressure in the arteries. The patient will complain of severe discomfort. Take now a large-bore needle, and pierce the ante-cubital vein—the blood will pour in a strong stream from the needle; it will start to pulsate later on, and the discomfort of the patient will diminish. The whole circle of blood circulation is engaged, the capillary bed is widely open, the pressure in all sectors is nearly equal. The capillary bed—the great buffer, and very active in its own right as well—is the deciding factor in what was discussed. This will explain what we see in the eye.

When the arteries on the disc start to collapse and fill up, as mentioned before, the incoming pulse-wave with still more increased pressure can be followed, say a disc-diameter, in the primary branches, but these branches never collapse. Why do they collapse on the disc? First, because the blood column is still able to force itself a short distance to the periphery within the primary branches, as can be seen by red-free light. Secondly, because I believe that in the disc the vessels are under increased pressure, being already caught between the substance of the disc and the special membrane covering the disc and described by Krückman. But further to the periphery the blood column cannot flow quickly, as it has to meet and to overcome the great regulator-buffer of the retinal capillary bed. We see in the eye what we only imagined going on under the cuff of the sphygmomanometer, but with one difference. There is always an escape from the venous blood through the veins on the disc. That is why the venous pulse is intensified in our experiments; the veins become narrower and then collapse completely, while the entrance of the blood into the arteries is stopped by our pressure. With increased resistance the pressure in the ophthalmic artery rises (a well-known phenomenon of local angiospasm—a defensive reaction), the increased force of the pulse wave is transferred from the arteries

to capillaries and from them—partly passively but chiefly actively —to the veins. It is this constant pressure on the inside of the capillaries—a very active force—that prevents the retinal arteries from collapsing, no matter how great is the external pressure. Theoretically, if a large-calibre cannula could be introduced into the veins in the disc, so that venous blood could flow out independently of the intra-ocular tension, the arteries on the retina would probably collapse.

In the retina we have to deal with a specially constructed pressure system with one narrow entrance and one narrow exit. Why do not the veins become blackish and tortuous during this experiment? Tortuous or flattened, as in glaucoma, they could become, but the time is too short, and they are not diseased, as they may be in glaucoma. They cannot become blackish, because there is no permanent obstruction, as in thrombosis, neither is the venous pressure raised in the ophthalmic vein, as in asthma, etc.

When the artery collapses on the disc, but still remains full of blood on the retina, just outside the disc, what prevents the blood from trickling back to the disc during the diastole, and so prevents the artery from collapsing? Even immediately after death it does not happen, but the blood eventually trickles back towards the heart later on. In a boy who died from advanced aortic insufficiency, I saw it happen within a minute or two of his death. The arterial system is full of blood, and the *vis a tergo* is a combination of the heart action and that of the muscular wall of the artery, distended by the blood column and the pulse waves, always tonically contracted and prepared to close the artery completely, if opportunity presents itself. It is therefore the contraction of the muscular coat of the primary branches that moves the blood ever forward away from the heart, and does not allow any backflow.

Summary

A full description of the artificially-produced retinal pulse is given, and the impossibility is noted of collapsing the retinal arteries in contrast with those on the disc. This remarkable fact, hitherto observed only by Baillart, but not explained by him, is analysed and explained by the active buffer-action of the retinal capillary bed.

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FACULTY TOUR OF SCANDINAVIAN CLINICS

TWENTY members of the Faculty of Ophthalmologists, led by Mr. W. M. Muirhead, sailed from Harwich on June 10. When they disembarked at the same port on June 28, nearly every one had increased his girth, and all were richer in experience. No ophthalmologist could help being thrilled to see the hospitals where Rönne and Bjerrum did their work, and to stand beside Gullstrand's rocking-chair. That we should have been able, in little more than a fortnight, to visit six illustrious clinics, sail upon the Baltic, and walk in the garden of Linnaeus, is proof of Mr. Muirhead's genius for organisation. It was he who planned the tour, greatly to the advantage of his colleagues.

Denmark

Professor Ehlers and his assistants showed us the ophthalmic and some of the other departments of the Rijkshospitalet. After the professor had made a speech of welcome, he let us hear about some of the recent investigations pursued. Dr. Johansen described his pathological studies upon enucleated eyes, and Fru Braendstrup spoke of a method whereby the temperature of the superior fornix can be shown to exceed that of the inferior by about 0.75°C. A refinement of technique in scotometry was the subject of Dr. Holm-Pedersen's paper. His three-faced test-objects — black, white and red — keep the patient "on his toes," because the object can be made to disappear (*i.e.*, go black) anywhere on the screen. Dr. C. Edmund spoke of his preliminary research upon endogenous and exogenous factors governing the light-reflex of the cornea. Then came Mr. H. Campbell-Orr's fundus photographs and Mr. P. Jameson Evan's films showing (a) the insertion of a slip of the internal rectus into a paretic superior rectus, and (b) grafting of the outer halves of the superior and inferior recti into a paretic external rectus, together with recession of the internal rectus.

Professor Holm welcomed us to his department at the Kommunehospitalet, told us about the hospital's development, and demonstrated a number of cases. Dr. Erik Godtfredsen showed a case of naso-pharyngeal sarcoma complicated by left abducent palsy. No cervical gland metastases were found, but the diagnosis was confirmed by X-ray photographs. A case of bilateral uveo-parotid fever in a girl of 17 was also shown by Dr. Godtfredsen, who recalled with interest that Heerfordt was First Assistant in this clinic when he produced his classical description of uveo-parotitis 40 years ago. Dr. P. Braendstrup spoke about amblyopia, with special reference to its association with traumatic cataract, and he produced

statistics showing that amblyopia is seldom acquired after childhood. A case of siderosis was demonstrated by Dr. C. J. Möllenbach.

We also attended a meeting of the Danish Ophthalmological Society at the Domus Medica under the presidency of Professor Ehlers, who proceeded to confer honorary membership upon Sir Stewart Duke-Elder. Sir Stewart had also been created an Honorary Member of the Swedish Ophthalmological Society during its Annual Congress a few days previously. Papers were then delivered. Mr. R. C. Davenport spoke about glaucoma in association with high myopia, and Dr. H. Skydsgaard dealt with the problem of word-blindness. Mr. J. H. Doggart described several cases of central serous retinopathy, and Mr. C. D. Shapland produced an analysis of his results in the treatment of detached retina. Finally Dr. A. Lund described his experimental work upon the intra ocular circulation.

Sweden

Professor Larsson, who had recently returned from a visit to the United States, showed us his famous clinic in Lund, and described his researches upon lenticular metabolism by means of fluorescence estimations. He also testified to the value of anticoagulants — notably dicoumarol—in the treatment of retinal venous thrombosis. Other subjects considered by Professor Larsson were the extraction of non-magnetic intra-ocular foreign bodies, and the treatment of infantile epiphora. Dr. A. E. Maumenee's film of intracapsular extraction, and Dr. R. Townley Paton's film of keratoplasty for corneal scar and for Descemetocele were shown. Dr. G. Österlind discussed the effect of milk injections upon the intra-ocular pressure, and Dr. E. Palm gave an account of his studies on the permeability of the blood-aqueous barrier to various substances, including lipoids. Mr. P. McG. Moffatt reviewed the differential diagnosis of proptosis, and stressed certain prognostic difficulties. Senile massive exudate at the macular was the subject of a talk by Mr. R. C. Davenport, who pointed out that retinitis circinata is not a clinical entity, but rather an incidental feature of certain conditions — notably senile massive exudate at the macula.

At Uppsala Professor Berg is occupied with administrative work as Rector Magnificus of the University, but he nevertheless found time to welcome us and to lead the social activities. He delegated the task of showing us the Department of Ophthalmology to the acting professor, Dr. Gunnar von Bahr, who afterwards gave a thoughtful discourse on spherical and chromatic abberration of the eye, and their effect upon human vision. Dr. U. Halldén spoke about fusional phenomena in anomalous correspondence, and the possible influence of this factor upon squint surgically treated. Dr. E. Linner discussed the work of Ascher and Goldmann on aqueous veins, and

its relation to the measurement of pressure in the anterior chamber and in Schlemm's canal. Dr. K. H. Sjöström described a case of lightning-cataract, and reviewed the ocular changes arising from electric shock. An account of anterior lenticonus in a 19-year-old male was given by Dr. C. G. Åborg.

Professor G. Karpe, who has recently been appointed to the Chair of Ophthalmology at the Karolinska Institute, Stockholm, conducted us around its palatial hospital. He described his technique of electroretinography, and indicated ways in which this method of investigation can assist the prognosis, especially in cases of retinal detachment. Professor Karpe also showed some fundus photographs taken with the Nordenson camera, and we were afterwards privileged to meet Professor Nordenson himself. Dr. T. Kornerup described his investigations upon the living eye with the aid of spectrally restricted light. Various structures can be selectively displayed by green, red and other kinds of light, and he demonstrated the apparatus by which light is shattered by a prism, and the required spectral component filtered through a slit. Dr. K. O. Grandström received us at the no less palatial Södersjukhuset, and gave an account of his clinical observations upon cataract, glaucoma, arterial hypertension, intra-ocular foreign body and toxoplasmosis. Dr. W. Magnusson showed us some fine X-ray photographs.

At Göteborg, Dr. H. Rosengren spoke about his work on retinal detachment, and described his technique for injecting air into the vitreous. Afterwards he demonstrated this process on the operating-table. Mr. Harold Ridley gave a talk on tropical ophthalmology, and emphasised the appalling havoc wrought by onchocerciasis upon Central Africans. Dr. H. Sjögren's subject was keratoconjunctivitis sicca, whose causation is not yet fully understood, though infection and endocrine dyscrasia appear to be the principal agents. Dr. S. Holm also gave a talk on Sjögren's disease. Physiological optics was the subject of a paper by Dr. Stenström, and Dr. S. Holm underlined the importance of heredity as the main aetiological factor in refraction.

Norway

Professor Malling, who welcomed us at the Rikshospitalet, Oslo, performed two cataract extractions, and gave a talk on exfoliation of the anterior lens capsule. He maintained that, although such exfoliation is often associated with glaucoma, it is not these exfoliated particles which cause blockage of the filtration angle. Dr. M. Haarr spoke about periphlebitis as a sign of multiple sclerosis. This vascular change is ophthalmoscopically visible, he says, in the form of white infiltrates around the retinal veins anywhere except in the juxtapapillary region. Dr. O. Röe's subject was methanol-poisoning.

He mentioned the favourable effect of sodium bicarbonate administered in the first three days, and the influence of ethyl alcohol in restricting damage from adulterated liquor. Dr. H. P. Petersen stressed the possibility of extensive colloid degeneration in the retrobulbar portion of the optic nerve, and adduced such a change as the explanation for certain cases of field-defect associated with but explained only in part by colloid bodies ophthalmoscopically visible. He suggested the simile of an iceberg, whose hidden bulk is more menacing than its exposed pinnacle.

Conclusion

Mr. Muirhead would be the first to point out that no plans, however carefully laid, can set the seal of success upon a tour. Success can only be attained by the interaction of friendly hosts and appreciative guests. Let it therefore be stated — and stated emphatically — that nobody capable of gratitude could fail to be touched by the welcome extended to us by Dane, Swede and Norwegian alike. Scandinavian hospitality is proverbial, so that we had naturally expected to enjoy those Northern lands, but the result surpassed expectation. The heads of all six clinics, together with their assistants, senior and junior, accorded us the freedom of their departments. They also flung wide open the doors of their homes, in which we passed many an hour of happy, informal talk. Kinder hostesses it is impossible to conceive, and we who were privileged to enjoy their hospitality will never forget how largely the success of the Scandinavian Tour was due to their welcome.

OBITUARY

H. H. McNABB

We regret to record the death of Dr. H. H. McNabb, M.D., which occurred at his home at Prestbury, Cheshire, last month at the age of 74 years.

Harry Horsman McNabb was born and received his early education in Bolton, later passing on to the University of Manchester, where he qualified M.B., Ch.B. in 1898, taking the M.D. four years later. After a short period in general practice, he was appointed a resident at the Manchester Royal Eye Hospital and subsequently Assistant Honorary Surgeon, full Surgeon, Consulting Surgeon and Vice-President, his connection with the Hospital covering a period of 49 years. During most of this time he conducted an extensive

private practice, and his services were much in demand as a medico-legal expert witness. He was an active member (and ex-President) of the North of England Ophthalmological Society and an enthusiast at the Oxford Ophthalmological Congress, which he attended regularly.

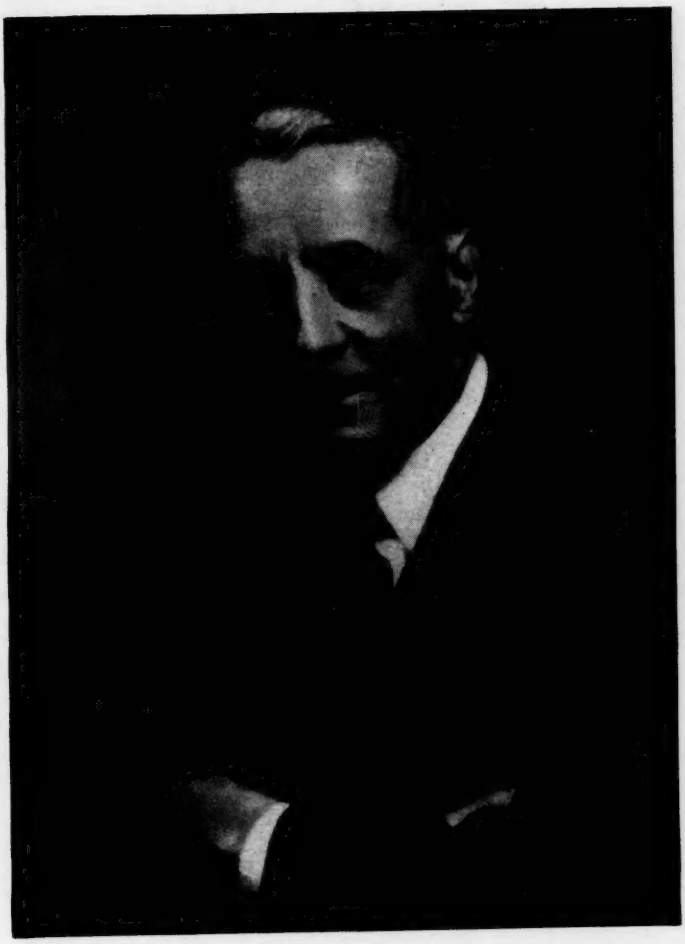
In spite of a busy, and at times overburdened, professional life, McNabb had varied hobbies. In his younger days he was a keen cricketer, and continued to take a great interest in the game, even when he ceased to participate actively in it. He was an expert fisherman, was something of an authority on roses, a keen bridge player, and, before the last war, travelled considerably abroad. The writer remembers dining with him one night, and on his table was a set of dinner mats—ink on white silk—of the old halls of Cheshire, most beautifully drawn by him, craftsmanship of the highest order.

Never physically robust, his health broke down in his early forties when he developed an active tuberculous chest lesion. He made an excellent recovery, but of necessity he lived subsequently a more limited life, which at times must have proved irksome, though he never complained of his ill-fortune. His last illness began some eighteen months ago, though mercifully he was saved a long period of pain and sueffring.

To his many friends, his colleagues and his patients, the keynote of his character was his gentleness and kindness. Never ruffled, never cross, always considerate and always willing to help a colleague —particularly a junior one—and to encourage his progress. As a clinical ophthalmologist he was in the front rank: a keen observer, an astute diagnostician, and so often in a difficult case able "to pull something extra out of the bag." His colleagues, who were fortunate to see his work, will perhaps remember most his superb operative ability. His fingers and his touch were perfect. It must be remembered that a great part of his operative life was spent in the days before the advantages of modern local anaesthesia were developed, and when the preparation of a patient consisted solely in the local instillation of a few drops of cocaine. In the ordinary sense he never seemed to operate on an eye—his fingers were so delicate and his touch so perfect. Even in those early days his patients were rarely restless, for he conveyed to them not only confidence but something of his own gentleness of character. It is a misfortune that no film of his operative work exists, for had it been so, it would have gone down to posterity as the perfection of our operative art. His colleagues will miss him sadly, but will remember him with affection and respect.

To his widow and his surviving son we offer our deepest sympathy.

O. M. D.



H. H. McNABB.

JOHN ROBERT FOSTER

BORN in Sleights, Yorkshire, in 1868. John Robert Foster qualified at Edinburgh in 1893. After holding House appointments at the Central London and Royal Westminster Ophthalmic and at the Golden Square Nose and Throat Hospitals, he was appointed as Ophthalmic Surgeon at the Hartlepools Hospital. A year later he was appointed as Ophthalmic Surgeon to the Cameron and Howbeck House Hospitals and the Hartlepools Education Authority as Aural and Ophthalmic Surgeon. He served in this capacity, being an excellent and careful surgeon, until at the age of 64 he had to retire from hospital and private practice owing to ill-health. His death occurred suddenly at the age of 81, at Danby, on August 5, 1949. He is survived by a widow and three children, the eldest of whom is Ophthalmic Surgeon to the General Infirmary at Leeds.

J. F.

FRIEDRICH P. FISCHER

THE death of Friedrich P. Fischer on July 23, 1949, at the age of 52, robs ophthalmology of one of its outstanding research workers. Fischer's interest lay mainly in the basic sciences, particularly in physical chemistry. Much of his earlier work was summarised in his remarkable contribution on The Water Content of the Eye, published in *Documenta Ophthalmologica* in 1938. The bearing of this highly abstruse work on glaucoma and on retinal detachment is obvious, and though Fischer could give no final answer, the work he has done is a permanent contribution to an exceptionally difficult subject. An equally important contribution bearing on the same clinical problems is represented by his recent paper on The Mechanical Properties of the Eye and its Tissues. His investigations on mycellia have a direct bearing on detachment, whilst his studies on elasticity and rigidity may ultimately help to clarify the problems of glaucoma.

Fischer's professional career was twice interrupted by the emergence of the Nazi horror. After 1933 there was no room for Fischer and his like in a Germany where all civilised values had collapsed. Through the wisdom of Professor Weve, Fischer found a congenial home at the Clinic at Utrecht. When he went to Utrecht at the age of 36 he took with him an international reputation in his own sphere based on over 40 publications, and his subsequent industry brought lustre even to the Utrecht Clinic with its great traditions. The occupation of Holland by the Nazis in 1940 interrupted Fischer's career for a full five years. With the

help of the highly organised Dutch resistance movement, and several false passports, he managed to elude the Gestapo, learning in the process how to trap rabbits in the woods, and to subsist on stolen chickens and stream-water. In the four years that were left to him at the end of the war he returned with renewed enthusiasm to his single-hearted devotion to research. A man of wide culture, he contributed to the study of the history of ophthalmology, as shown by his excellent paper on Goethe. He became one of the editors, and the leading spirit, of the revived *Documenta Ophthalmologica* and of the ophthalmic volumes in *Tabulae Biologicae*. In his work he was greatly assisted by his wife and his colleague, Dr. H. von Bunau. To her and to their two daughters goes out the sympathy of the profession at large.

A. S.

NOTES

International Exchange of Publications

A MANUAL on the International Exchange of Publications will be published this year by Unesco Clearing House for Publications, 19, Avenue Kléber, Paris 16e. Annexed to this manual will be a classified list of institutions willing to exchange their own publications, or publications regularly at their disposal. Relevant details, which should reach Unesco by October 1, 1949, are (a) name and address of institution (*e.g.*, library, university, learned society); (b) titles of publications offered; (c) any special conditions of exchange.

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University of Toronto

THE Professor of Ophthalmology, Faculty of Medicine, University of Toronto, announces a 3-year post-graduate course in ophthalmology. Appointments are made in December, and work begins on the following July 1. A successful candidate is granted a special Fellowship worth approximately $1400, which enables him to devote the first year to one of the basic sciences of ophthalmology. He spends the other two years on the intern service of one or more of the University teaching hospitals, but must attend courses of instruction by members of the staff. Such teaching occupies about four hours a week from October to May, and the fee payable is $50 a year. Senior interns are taught how to prepare and deliver scientific papers.